INEQUALITY IN OUTCOME FOR OESOPHAGO-GASTRIC CANCER IN ENGLAND: IS THERE AN ASSOCIATION WITH GASTROSCOPY RATES IN GENERAL PRACTICE POPULATIONS?

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor in Philosophy

By

Mustafa H.M. Shawihdi

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Dedication

This thesis is dedicated to my parents (Mr Hussein Shawihdi and Mrs Amal Mustafa) and my wife Dr Hend Belhaj for their assistance, helpfulness and patience. It is also dedicated to my children; Huseen Shawihdi, Mohamed Shawihdi and to my special Baby that I am waiting for.

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Publication to date from this work

Bodger, K. and **M. Shawihdi** (2013). "Variation in referral practice and differential cancer outcome: a strong reason to reflect on whether current guidelines are fit for purpose or implemented effectively in primary care." Gut. **(Letter attached)**

Shawihdi, M., et al., PWE-068 Diagnostic Yield of Serious Disease and Variation in Elective Gastroscopy Rates in English General Practice: Analysis Of Administrative Data. Gut, 2013. 62(Suppl 1): p. A158. **This work awarded the British Society Of Gastroenterology's prize for BEST poster (Prize attached)**

Shawihdi M, Thompson E, Kapoor N, Powell G, Sturgess R, Stern N, Roughton M, Pearson MG, Bodger K. Variation in gastroscopy rate in English general practice and outcome for oesophagogastric cancer: retrospective analysis of Hospital Episode Statistics. Gut 2013. **(Paper attached)**.

M Shawihdi*, G Powell, N Stern, N Kapoor, R Sturgess, E Thompson, M Pearson, K Bodger. Gastroscopy rate in English general practice populations: association with outcome for oesophagogastric cancer. Gut 2012;61:Suppl 2 A19 doi:10.1136/gutjnl-2012-302514a.44

M Shawihdi*, N Stern, E Thompson, R Sturgess, N Kapoor, M Pearson, K Bodger. Emergency admission as a route for oesophagogastric cancer diagnosis: a marker of poor outcome and a candidate quality indicator for local services Gut 2011;60:Suppl 1 A30-A31 doi:10.1136/gut.2011.239301.61

This work presented in BSG , DDW and NCIN international conferences. Recently, it also attracted the following professional and public media interest.

Jacqui W. GP practices with low referral rates for gastroscopy put patients at risk of worse outcomes, research shows. Bmj 2013;346 **(News attached)**

Donnelly L. Postcode lottery of patients' risk of dying from cancer. The Telegraph .Availableonline:http://wwwtelegraphcouk/health/healthnews/10116958/Postcode-lottery-of-patients-risk-of-dying-from-cancerhtml; 2013

Inequalities in outcome for oesophago-gastric cancer in England: Is there an association with gastroscopy rates for General Practice populations?

Abstract: Mustafa Shawihdi

Introduction: Oesophago-gastric (OG) cancers remain a worldwide challenge with little sign of major improvements in survival rates. Modern guidelines focus on alarm (or 'red flag') symptoms as key triggers for gastroscopy and recommend empirical symptomatic treatment and non-invasive *H. pylori* testing in those with simple dyspepsia. However, the early symptoms of OG cancer are very common and non-specific, and the traditional alarm symptoms have poor sensitivity or specificity for malignancy. Diagnosis therefore necessitates investigation of symptoms though upper GI endoscopy in a relatively large group of patients, most of whom do not have malignant disease. This has fuelled considerable controversy regarding the role for gastroscopy in detecting cancer at a treatable stage.

Objectives: Firstly, to develop data extraction and linkage methods for studying OG cancer outcome, and General Practice population rates of elective diagnostic gastroscopy, using administrative data for English hospitals (Hospital Episode Statistics). Secondly, to confirm the face-validity of the methodology using external sources of information and local audit data. Thirdly, to test the hypothesis that variations in rates of gastroscopy in English General Practice (GP) populations are associated with inequalities in OG cancer outcome. Fourthly, to explore whether practices with lower rates of gastroscopy exhibit a higher yield of serious pathology, consistent with more selective referral practice. Fifthly, to confirm the existence of wide variation in gastroscopy rate between practices in close geographical proximity,

Design and methods: Analysis of Hospital Episode Statistics (2006-8) linked to death registry and practice population data. General practices with new cases of OG cancer were included, grouped into tertiles according to standardised elective gastroscopy rate per capita (low, medium or high). Outcome measures for cancer cases were: emergency admission during diagnostic pathway; major surgical resection and mortality at 1 year. Co-variates were age, gender, co-morbidity, and deprivation. Associations between the gastroscopy rate at the patient's general practice and cancer outcomes were tested in binary logistic regression models, with extensive sensitivity testing of gastroscopy rate 'exposure' variable. An algorithm was developed to analyse coded diagnoses for all first elective gastroscopies, using both national and local audit data. Practices were mapped based on postal code.

Results: 22,488 incident cases of OG cancer from 6,513 general practices. Mean OGD rate for Low, Middle, High practices: 4.4 vs 8.1 vs 12.9 per 1,000. Mean age of patients undergoing OGD was highest for low tertile practices (60.2 vs 59.5 vs 58.4 yrs; $p<0.001$). OG cancer cases registered with practices in the lowest tertile had the lowest rate of surgery (15.4% v 16.3% v 17.4%; $p=0.004$) with the highest rate of emergency admission (34% v 26% v 25%; $p<0.001$), and the highest mortality (61.2% v 58.9% v 58.0%; $p<0.001$). After adjustment for co-variates in logistic regression, the gastroscopy rate at the patient's general practice was an independent predictor of all three outcomes. Practices with low rates of gastroscopy tend to have a higher "diagnostic yield" of serious disease: (15.3% vs 13.9% vs 13.1%; $p<0.001$). Low tertile practices also showed a relatively lower referral rate for suspected cancer in general based on analysis of rates of 'fast-track' referrals under the two week wait pathway (17.3 vs 17.9 vs 19.3 per 1,000).

Conclusions: Wide variation exists in gastroscopy rate among general practice populations in England. OG cancer patients belonging to practices with the lowest gastroscopy rates are at greater risk of poor outcome. Low referring practices achieve a higher yield of serious disease but may have increased risk of referral at a later stage in the disease process. This association is more apparent among the most socially deprived practices. These findings suggest that initiatives or current guidelines aimed at limiting the use of gastroscopy may adversely affect cancer outcomes.

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List of abbreviation

abbreviation	Description
OG cancer	Oesophago-Gastric Cancer
TWW	Two week wait
RAUGICS	Rapid Access Upper GI Cancer Service
OG junction	Oesophago-Gastric (OG) junction
GORD	Gastro-Oesophageal Reflux Disease
GI	Gastrointestinal
OGD	Upper gastrointestinal endoscopy
OAG	Open access gastroscopy
JAG	Advisory Group on Gastrointestinal Endoscopy
H. Pylori	Helicobacter pylori
PPI	Proton pump inhibitor
H2-RA	H2-receptor antagonists
GP	General practitioner
GP practice	General practice
PCT	Primary Care Trusts
SUS	Secondary Uses Service
PAS	patient administration systems
HES	Hospital Episode Statistics
FCE	Episode of care or Finished Consultant Episode
HESID	The identifier that is unique to each patient and his/her HES records
ICD	International Statistical Classification of Diseases
OPCS	Office of Population, Censuses and Surveys Classification of Interventions
DIAG01	Position of the Primary diagnosis code in HES
DIAG02-DIAG14	Position of the secondary diagnosis codes or associated co-morbidity in HES
OPERTN01	Position of the Primary procedure code in HES
OPERTN02-OPERTN14	Position of the secondary procedure code in HES
IMD	Index of Multiple Deprivation
LSOA	Lower Super Output Area
SD	Standard deviation
CI	Confidence interval
OR	Odd ratio
$\chi 2$	Chi-square
ANOVA	Analysis of variance
UK	United Kingdom
WHO	World Health Organization
NHS	UK national Health Service
BSG	British Society of Gastroenterology
RCGP	Royal College of General Practitioners
RCP (*i*Lab)	The Royal College of Physicians Information Laboratory
NCIN	National Cancer Intelligent Network
ONS	Office of National statistics
HSCIC	Health and Social Care Information Centre
NICE	England and Wales National Institute of Clinical Excellence
SIGN	Scottish Intercollegiate Guidelines Network
ACG	American College of Gastroenterology
AGA	American Gastroenterological Association
CanDys	Canadian Dyspepsia Working Group
STROBE	Strengthening the reporting of observational studies in epidemiology

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Chapter 1 Introduction and general overview

1.1 Oesophago-gastric cancer background

Oesophago-gastric cancers (OG cancers) are tumours which arise from the oesophagus or stomach, respectively. These two cancer sites exhibit a very similar age profile at diagnosis, present with an overlapping range of symptoms and signs, and share a common diagnostic pathway centred on a key primary diagnostic test (gastroscopy). They are often referred to, collectively, as upper gastrointestinal cancers.

1.1.1 Anatomical description of the oesophagus and stomach.

The oesophagus is a muscular tube that lies at the front of the spine and behind the trachea. It carries swallowed food through the neck and chest to the stomach. This tube in a human adult is usually about 18 to 26 cm long and around 2-3 cm in diameter at its smallest point.[1] The oesophagus unites with the stomach at the *gastroesophageal junction*, located just beneath the diaphragm. The stomach is a J-shaped (sac-like) muscular organ that mixes and digests food by secreting gastric juice and then emptying it into the *duodenum,* which is the first part of small intestine [1] **(Figure 1.1) .**

Figure 1.1 also shows the wall of the oesophagus and stomach, with its several layers. These layers are important for an understanding of where cancers tend to start and the staging of the disease, which will subsequently inform the management of the disease, as will be described later.

1.1.2 OG Cancer pathological subtypes.

The vast majority of oesophageal cancers that emerge from oesophageal tissue are epithelial tumours which originate at the mucosa and grow through the submucosa and the muscle layers.[1] Since two types of cells can line the oesophagus **(Figure 1.1)**, there are correspondingly two main types of oesophageal cancer, namely squamous cell carcinoma and adenocarcinoma of the oesophagus and the oesophago-gastric (OG) junction.[1, 2]

This text box is where the unabridged thesis included the following third party copyrighted material:

Cancer research UK. 18/06/13 [cited 2013; Available from: http://www.cancerresearchuk.org/cancerinfo/cancerstats/types/oesophagus/incidence/uk-oesophageal-cancer-incidence-statistics.

Figure 1.1 Normal structure of oesophagus and stomach adapted from cancer research UK. [3]

About 90% of gastric tissue malignancies are Adenocarcinoma.[4] Other less common epithelial and non-epithelial cancers include squamous cell carcinoma variants, small cell carcinoma, malignant melanoma, lymphomas, sarcomas, neuroendocrine tumors, and secondaries from other sites (for example, breast cancer as the primary site) [2, 5].

Squamous cell carcinoma tends to occur in the upper and middle (thoracic) part of the oesophagus. This used to be the most common variety of oesophageal cancer type, particularly in men with a long history of smoking and alcohol consumption.[1, 6] Adenocarcinoma appear to affect mostly white men, and its pathogenesis is thought to be related mainly to gastro-oesophageal reflux disease (GORD) and the development of Barrett epithelium, as will be discussed later [6-9].

1.1.3 Oesophago-gastric cancer epidemiology.

Over the last few years, the incidence of adenocarcinoma of the lower oesophagus and gastro-oesophageal junction has increased dramatically [1, 6]. In some Western countries such as the UK and the USA, this type has now overtaken squamous cell carcinoma to become the dominant histology at diagnosis [4, 6], to the extent that in the year 2000, the world's highest estimated incidence rate of adenocarcinoma was recorded in the UK, at a rate of 8.7 cases per 100,000 population. [8] In the USA, throughout the 1980s, adenocarcinoma of the oesophagus increased at a rate of 5 to 10 % per year.[10] Another study from Norway has also reported a substantial increase in the incidence of this malignant tumour, at a rate of 15% per year[10].

A similar pattern of rising incidence, particularly around the gastro-oesophageal junction, has been widely reported in various other countries, including Sweden, Switzerland and Australia.[11] More recent UK figures show that the crude incidence rate of oesophageal cancer are 18.4 per 100,000 population for males and 9 per 100,00 0 for females. [12]

There were 83,000 new gastric cancer cases in Europe in 2008 with a UK incident rate being below the European average at about 12.4 per 100,000 in males and 5.3 per 100,000 in females.[13] In the UK, the trends of gastric cancer incidence have fallen dramatically by about 32% in males and 28% in females, comparing the period of 1999-2001 with 2008-2010.[13]

UK data from the mid-1990s also shows that there were around 7000 and 10000 new diagnoses per year, and these were responsible for about 6700 and 7500 deaths for oesophageal and gastric cancer respectively.[14] In more recent times, during 2005-2007, ONS data demonstrates that around 7919 and 7897 were newly diagnosed, with mortality figures of 7336 for oesophageal cancer and 5395 for gastric cancer. [15]

Although the incidence of adenocarcinoma of the oesophagus is increasing, and the incidence of gastric carcinoma is decreasing [4], nevertheless gastric cancer remains the fourth most common cancer and the second main cause of cancer death throughout the world, [5] while oesophageal cancer ranks as the eighth most common cancer worldwide.[6] In the UK, however, it is ninth, and is grouped with gastric cancer (OG cancer) as the fifth most common malignancy and fourth most common cause of cancer death [5, 16-19].

There are significant geographic and regional variations in the incidence of OG cancer around the world.[6] Gastric cancer for instance is very common in China, Japan, Eastern Europe and South and Central America while it is uncommon in Northern and Western Africa.[4] There was also a fourfold difference in the incident rate of gastric cancer in EU counties.[13] These differences may imply that genetic, environmental and lifestyle factors play an essential part in the aetiology of these cancers, as has been widely suggested. [2, 10, 20, 21]

Generally, OG cancers remain a worldwide challenge with little sign of major improvements in patients' outcomes. Taken as a whole, the 5-year survival rate in

England and Wales is about 13 per cent for gastric and 7 per cent for oesophageal cancer [2, 16, 22]. However, better survival rates have been found in some areas where patients have been diagnosed at an early stage of the localized disease [22]. These variations could also reflect the type and quality of the cancer management and services provision in these areas.

It has been reported that survival rates of OG cancer in England are worse than the European average, and noticeably poorer than rates achieved in Japan and the USA.[17] This is most obvious for patients with gastric cancer, whose one year survival rate is 40 per cent across Europe as a whole, compared with 28 per cent in England **(Table 1.1).** [10]

Table 1.1 One and five years survival rates, with 95% confidence intervals (CI), among patients with OG cancers in England and Europe. Adapted from Guidance on Commissioning Cancer Services, Improving Outcomes in Upper Gastro-intestinal Cancers. 2001 [10]

Although the survival of cancer patients is considered an important index of the overall effectiveness of health services, it has been argued that international comparisons both within and between countries that have comparable health systems and wealth, such as Denmark and the UK and other European countries, may not be entirely reliable [23, 24].

"With regards to their point that the UK lag in survival is "frightening for NHS patients and demoralising for NHS staff," we instead suggest that the data are encouraging for the UK. EUROCARE-4 was concerned with patients diagnosed in 1995–99, and clear improvements in UK survival were seen compared with in 1990–94. The National Cancer Plan for England was implemented in 2000 and the expected favourable effect will only be visible in patients diagnosed after that time." [2]

However, these survival statistics were drawn from data obtained from the Eurocare project, which now involves over 80 cancer registries across 23 countries.[25-28] Furthermore, various high resolution studies have used these data to explore the influence of disease stage at diagnosis and of treatment, providing some possible explanations for such variation in survival rates.[28-31] Thomson CS et al (2009) for instance in a comparative analysis of the Eurocare 4 data acknowledged some cancer sites, including oesophagus where the one year survival was a significant factor in 5-year survival, and thus where an earlier cancer diagnosis would create a significant difference.[30] Across Europe, Bouvier et al (2010) also showed that differences in gastric cancer survival largely depend on differences in stage at diagnosis rather than on quality of treatment.[29] The size of the prize publication by Sir Mark Richard in 2009 concludes that UK diagnostic delay may help explain an estimated 5,000-10,000 additional cancer deaths each year.[32] To put this into perspective, Abdel-Rahman et al (2009) point out that OG cancers would have one of the highest numbers of 'avoidable' deaths, if cancer survival in Britain could reach the same levels as elsewhere in Europe.[33]

These figures support the argument that many cancer deaths could be avoidable simply by improving patients' care pathway.[23, 24] Although these variations might reveal the type and provision of the cancer management in general, it might also reflect the inadequate availability, or the poor access to diagnostic services in these areas. In addition, it is still unknown whether these variations could result from the early/late specialist referral of patients who are found to have nonspecific symptoms.

1.1.4 Risk factors for developing oesophago-gastric cancer

Illness related risk factors are anything that has an effect on an individual's chance of contracting the disease. [34] In the case of cancer, the risk pattern is complicated. Different cancers have different risk factors, while some may not have a known risk factor at all. It is important to note that having one or more risk factor does not indicate that the individual will necessarily develop the disease.[34]

1.1.4.1 Patient demographics (Age, gender and race)

Although oesophago-gastric cancers age distribution shows variations in some definite geographical distinct areas of the world [35-38]; generally, the chance of developing these cancers is low at younger ages and the risk is much greater in elderly people.[1] In the UK, 92% of new cases occur in those more than 55 years of age.[39] During the sixth and seventh decades of life oesophageal cancer is approximately 20 times more common than in those under 65 years. In the same way, in men above 80 years of age, gastric cancer peaks at 200 cases per 100,000 individuals.[10, 40]

Around two-thirds of OG cancers cases are found in men. Recent figures from the Office for National Statistics (ONS) show that the directly age-standardised rate of newly diagnosed cases of oesophageal cancer for men and women in England is 13.9 and 5.5 per 100,000, respectively.[15] The same source also records that the gastric cancer incidence for men is 13.3, while in women it is 5.3 per 100,000 population.[15] ONS data also shows that the mortality rate from these cancers is considerably higher in men than in women at 12.9 to 4.7 deaths per 100,000 population for oesophageal cancer and 8.5 to 3.6 per 100,000 population for gastric

cancer.[15] Although it is still unclear why men are at greater risk of both developing and dying from those cancers, it has been argued that more proactive health care approach need to be adopted in relation to men's increased vulnerability to cancer in general.[41]

Although researchers have hypothesized that environmental factors, such as differences in lifestyle and smoking, might account for this gender discrepancy, an increased body of evidence suggests that these variations might be deeply rooted in the biological differences between men and women.[42] For example, Sheh et al showed that treating male mice with estrogen significantly reduces their rates of stomach cancer caused by *H. pylori* chronic infection.[42]

It is also likely that ethnicity might be one of these cancer risk factors. In the United States, for instance gastric cancer is shown to be more common in African Americans and Hispanic Americans than in non-Hispanic whites. It was also reported as prevalent among Asian/Pacific Islanders.[1] In England, differences in the incidence of oesophageal and gastric cancer have been reported at similar rates among various ethnic groups,[43] and this relative homogeneity has been suggested as being due to exposure to other risk factors.[43]

1.1.4.2 Gastro-oesophageal reflux disease (GORD) and Barrett's oesophagus

GORD related symptoms in terms of *heartburn and acid regurgitation* are considered one of the most common complaints in the General Practice setting.[44] The prevalence of this clinical condition varies greatly, although in Western world it ranges between 10 to 20%. [44, 45] In the UK, the incidence and prevalence of

GORD, when defined as at least weekly heartburn and/or acid regurgitation, were 4.5 per 1000 person-year and 18% respectively.[45, 46]

It has been shown that the frequency or severity of GORD symptoms could be sufficient to disturb the patients' health-related quality of life [45, 47]. Reflux of gastric contents into the oesophagus could damage its squamous cell lining and associated serious complications, including erosive oesophagitis, oesophageal stricture and the risk of developing adenocarcinoma of the oesophagus and/ or gastroesophageal junction have been extensively reported in the literature [44, 48-51].

If reflux of gastric contents into the oesophagus continues over a long period, this causes the lower oesophageal squamous cells to be replaced with glandular (columnar) cells.[1] These columnar cells are similar to gastric and/or small intestinal cells which are more resistant to gastric acid. This condition is known as Barrett's oesophagus. [52]

Barrett's oesophagus is found to be an uncommon (1% to 2%) finding at endoscopy.[1, 53] For symptomatic GORD, such a finding could however be as high as 12%.[53] It has been reported that patients with Barrett's are at around 11 times higher risk of developing adenocarcinoma of the lower oesophagus than in the normal population.[54]

1.1.4.3 *Helicobacter pylori* (*H. pylori*) infection

H. pylori was first reported in 1984 by Robin Warren and Barry Marshall.[55] Since then, a substantial number of studies and review articles have provided

considerable evidence that infection with *H.pylori* plays an important role in gastric cancer pathogenesis.[56-59] The fall in gastric cancer incidence in developed countries has been linked to the eradication treatment and a decline in the prevalence of *H.pylori* infection in these areas.[11, 60] Meta-analyses of prospective studies have suggested that chronic *H pylori* infection increases the risk of gastric cancer by 2-3 times.[61, 62] It has been shown that *H. pylori* has a strong link with dyspepsia and may be accountable for at least 5% of upper GI symptoms in the community.[63]

A project conducted by the *Helicobacter* and Cancer Collaborative Group combined twelve case control studies to measure the relative risk of gastric cancer in association with *H. pylori* infection. It found that that those with *H. pylori* infections are 5.9 times more at risk of developing non-cardia gastric cancer.[64] However, this study also reported that *H pylori* does not increase the risk of gastroesophageal junctional (*cardia*) tumours. [64] Brewster suggests that the fall in *H. pylori* prevalence presents a possible explanation for the growing incidence of adenocarcinoma of the oesophagus and gastric cardia, and the declining incidence of distal gastric cancers.[65]

Furthermore, certain types of lymphoma of the stomach, known as mucosa-associated lymphoid tissue (*MALT*) lymphoma, have been shown to be caused by *H.pylori* infection which is entirely treatable with antibiotic eradication therapy.[1, 66].

This text box is where the unabridged thesis included the following third party copyrighted material:

Burkitt, M., Investigation of the importance of individual members of the Nuclear Factor-κB family during Helicobacter felis induced gastric carcinogenesis, in Gastroenterology2011, University of Liverpool.

Figure 1.2 adapted from Burkitt et al 2009, shows how the development of gastric cancer is one of several potential outcomes of chronic gastric colonisation with *H.pylori* infection. [67]

1.1.4.4 Alcohol and tobacco

Alcohol drinking and the use of tobacco products, such as cigarettes, chewing tobacco and pipes, are well recognized risk factors for squamous cell carcinoma of the oesophagus, particularly in most low risk countries.[68] However, their relation to oesophago-gastric adenocarcenoma remain unclear. [11, 69] A meta-analysis of published studies, carried out to examine the gastric cancer risk associated with smoking status, demonstrated a relative risk of 1.48 (95% CI 1.28-1.71) for those that have ever smoked, in comparison to non-smokers.[70]

Studies have also shown a dose-and-time relation, in which the greater and the longer the use of tobacco and alcohol, the higher the chance of developing gastric cancer.[11] Additionally, It has been shown that smoking and drinking could have synergistic effects on OG cancer development, which may augment the relative risk

over time, compared with the effect of either smoking or drinking on its own.[71] However, various limitations of these studies have been noted, particularly the fact that their lack of control for possible confounding factors such as *H. Pylori* infection, or by the level of fruit and vegetable intake, which are both highly correlated with tobacco smoking.[11]

1.1.4.5 Diet and nutritional imbalance

Poor and/or under-nutrition includes the low intake of micronutrients such as vitamins, antioxidants and an above average consumption of foodstuffs such as smoked foods, salted fish and processed meat are shown to have an increased risk of OG cancer.[11, 71, 72] By contrast, a diet high in fruits and vegetables has been related to a reduced risk.[11, 71]

Another risk factor is over-nutrition, associated with high carbohydrate intake and obesity.[73-75] Although the exact mechanism for this correlation is still not fully understood, it has been partly explained by the finding that obese individuals are more likely to develop GORD.[1]

1.1.4.6 Socioeconomic status

Generally, the relations between social deprivation status and cancer incidence and survival have been well documented in the literature. [76-78] The risks of OG cancer have also been linked strongly with socioeconomic indicators. [76, 78, 79] On average, low socioeconomic status has been consistently shown to be associated with an increased risk of both oesophageal and gastric cancers [76, 78, 79]. However, analysis of cancer registry data from the West Midlands region of the

UK explores the relationship between the degree of deprivation and these tumours, with its sub-sites and subtypes. [80] The report showed that a higher percentage of cases of adenocarcinoma of the lower oesophagus and gastric cardia were among higher social class.[80, 81] Interestingly, it remains unproven whether smoking, alcohol, obesity, and/or the changing in the prevalence of *H pylori* infection are associated with OG cancer patients' socioeconomic status.[79] Such explanations would help to give more insight about the variability in the incidence of this particular cancer among people living in more deprived communities.[11, 65]

1.1.4.7 Other OG cancer risk factors

A number of conditions appear to be associated with an increased risk of oesophageal and gastric cancer.[1, 11, 82] These factors are summarized below **(Table 1.2).**

Table 1.2 Other risk factors for OG cancer

Oesophageal	Gastric
• Thermal and mechanical irritation or Injury to the oesophagus • History of certain other cancers • Achalasia • Tylosis • Oesophageal webs • Workplace exposures Chemical fumes	• Previous stomach surgery • A family history of stomach cancer • Pernicious anaemia • Epstein-Barr virus infection • Menetrier disease (hypertrophic gastropathy) • Immune deficiency • Common variable immunodeficiency (CVID) • Type A blood • Inherited cancer syndromes BRCA1 and BRCA2 Familial adenomatous polyposis (FAP) Hereditary non-polyposis colorectal cancer • Certain occupations Workers in the coal, metal, and rubber industries

Summary Box 1

Oesophageal and gastric cancers have been linked to various risk factors. Although some risk factors could be avoidable (such as drinking alcohol or smoking), others are beyond the patient's control, for example advancing age or family history.[34] The typical presentation of these tumours in older individuals has supported the use of arbitrary age cut-offs in referral guidelines to encourage the restriction of gastroscopy for simple dyspepsia to those over the age of 55 years. Only around 8% of gastric cancers, for instance, occur under the age of 55 years.

1.1.5 Clinical features

Symptoms that might be an indication of the presence of OG cancers are very common and non-specific. One such symptom is dyspepsia: around one fourth of the general population is described as affected with dyspepsia, without necessarily suffering from cancer, and it is estimated that dyspepsia accounts for around 5% of general practice consultations and about 30% of gastroenterologists' visits.[1]

2000 years ago, the Greeks coined the word "dyspepsia" for "bad digestion", which in English became simply "indigestion", a term which is widely understood by lay people as referring to any pain and/or discomfort in the upper abdomen. Such pain may or may not be associated with bloating, postprandial fullness, nausea, anorexia, heartburn, regurgitation, early satiety, and burping or belching.[1] Health professionals on the other hand, often use dyspepsia as a term to illustrate heterogeneous upper abdominal symptoms that could originate from organic causes, including malignancy, or which could originate from an inorganic, as yet unspecified source. [2, 83]

More recently, although there has been considerable progress in our understanding of the various clinical approaches to dyspepsia, nevertheless physicians continue to have difficulties in managing patients who present with such symptoms, partly because of the challenge of defining, investigating and treating dyspepsia. Because it is a symptom (or a group of symptoms) rather than a disease, doctors' interpretations of their patient symptom are highly affected by language, culture,

age, and past clinical experiences [2, 84]. Hence, an agreed standard definition of dyspepsia is essential in any given study relating to this universal clinical condition.[37] It has also been shown that variation in the prevalence of dyspepsia, which ranges from 15% in Asia to 40% in North America, were primarily due to differences in definition, rather than any significant medical differences in the geographical locations. [37]

In a longitudinal 10 year UK follow-up study, Ford et al. found that the incidence of new-onset dyspepsia was almost 3% per year. This study also showed that the nature of this clinical condition involves a remission and relapse period, and that previously asymptomatic individuals may experience a new onset of symptoms compatible with dyspepsia. For these reasons, even over a prolonged period of time, in the same demographic and geographical area the prevalence of dyspepsia tends to remain almost the same [85, 86].

More specific symptoms which if present, could be related to the presence of OG cancer are called “alarm or red flag symptoms” **(Table 1.3)**. However, research has consistently shown that these symptoms have low predictive value in unearthing serious findings at endoscopy.[87-89] Nevertheless, OG cancer is shown to seldom occur in young patients without alarm features. [90] Although these red flag symptoms are not uncommon in primary clinical practice, the number of studies which test the predictive value of each individual symptom, either alone or in combination, is small.[88, 91]

Table 1.3 Alarm features in dyspepsia that could suggest the presence of upper gastrointestinal malignancy. [83]

Fransen et al (2004) in a critical review of studies testing the diagnostic value of alarm symptoms in relation to OG cancer suggest that the sensitivity of 'any alarm symptom' as an indicator of malignancy is "*rather disappointing*" – a suggestion supported by the findings of Vakil et al (2006). Additionally, these meta-analyses indicate a low positive predictive value (PPV) for having these warning symptoms, demonstrating that an insignificant proportion of these cases actually have cancer. Although this low PPV might be related simply to the low prevalence of this cancer type, these studies also reveal a high negative predictive value (NPV), which indicates that there is small probability of missing an OG cancer in patients without these symptoms.[88, 89]

In relation to the disease staging, it appears that patients with alarm symptoms could have advanced disease at the time of presentation.[92] Previous studies have also reported that the majority (70%) of patients with early gastric cancer have presented with dyspepsia with no anaemia, dysphagia or weight loss. [93]

In this regard, Kapoor et al state that

"Unfortunately, the symptoms of early stage cancer may be indistinguishable from benign conditions, whereas the presence of established alarm symptoms (for example, dysphagia or weight loss) may signify advanced inoperable disease." Kapoor 2005 **[94].**

Summary box 2

Although some upper gastrointestinal symptoms or clinical features are considered more important than others as indicating risk for underlying OG cancer, the traditional 'red flag' or 'alarm' symptoms are an unreliable means of identifying patients with serious causes of dyspepsia. It is doubtful that a focus on alarm features alone promotes early-stage diagnosis for the minority of symptomatic dyspeptic patients with underlying cancer.

1.1.6 OG cancer Diagnosis and Staging

The World Health Organization (WHO) recommends that the diagnosis of OG cancer should be made by endoscopic biopsy with histological examination.[95-98] Neither signs, symptoms nor serologic markers may be 100 % indicative of the presence of OG cancer.

Gastroscopy allows for the direct characterization of the tumour's location, size and configuration.[1] It has also been recommended that at least six biopsies are typically required to yield a diagnosis. However, some centres may use the brush cytology to enhance the diagnostic yields. [1]

Although upper GI endoscopy with biopsy is the gold standard diagnostic investigation, irrespective of radiological image finding in patients who are suspected of having this malignancy, nevertheless contrast radiographic techniques (e.g. Barium) may also be required in selected cases, particularly in patients with suspected fistula and/or complete obstruction. In addition, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and endoscopic ultrasonography (EUS) are mandatory in evaluation of the surrounding tissues and to show the presence or absence of distant metastasis.[1, 96, 97]

The TNM classification system is used to measure how far a cancer has spread.[1] Various radiological and endoscopic investigations are involved to determine the most consistent information about each stage of this system. The main methods are multi-detector CT (MDCT), EUS and PET integrated with CT (PET-CT).[99]

Essentially, TNM gives details in relation to the **depth of tumour invasion** into the oesophageal or gastric wall (**T**). Studies show that, in small "early" T1 stage cancer, endoscopic mucosal resection (EMR) is the favoured approach for examining mucosal and submucosal invasion. In more advanced lesions; however, EUS is more precise, because of the defined visualisation of each layer of the oesophageal and gastric tissue.[1, 99]

With regard to the **association of lymph nodes** (**N**) and the **existence of distant metastases** (**M**); although, they are highly dependent on the anatomical location of the primary tumour, the highest possible accuracy has been achieved using a combination of EUS (alone or with CT) and/or PET-CT.[1, 99]

Since around half of patients present with advanced disease; according to the BSG's 2011 recommendation, any assessment ought to establish the existence or nonexistence of distant metastasis. Even though MDCT is the standard technique to rule out metastatic disease, all three modalities need to be applied in combination to offer complete staging detail. [99]

1.1.7 OG cancer treatment options

OG cancer therapeutic options are extremely stage dependent. Only those infrequent patients with early stage localized disease are suitable for primary treatment with curative intent, predominantly in the form of radical surgical resection. Such a minor group has a better opportunity for survival.

Primary treatment options include surgery alone, which is considered the mainstay curative modalities particularly for adenocarcinoma; chemotherapy with radiation

therapy, which has been shown to be an effective primary curative treatment for squamous cell carcinoma of the oesophagus; or combined modality therapy [10, 100]. Endoscopic mucosal resection (EMR) and photodynamic therapy (PDT) also offer an alternative to surgery, especially in the management of high grade dysplasia with an early cancer of the oesophagus or stomach. Additionally, EMR/PDT provides the advantage of low morbidity and mortality, combined with the preservation of normal digestion and quality of life, with a survival rate comparable to that of major surgical resection [100].

More recently, endoscopic sub-mucosal dissection is also judged to be a relatively safe and effective treatment, particularly for early and superficial gastric and oesophageal neoplasms. [101, 102]

Definitive chemotherapy in combination with radiotherapy, as another alternative to surgery, has also been considered by some especially for patients unfit for surgery; however they are associated with high morbidity [2, 103].

Combined modality therapy (chemotherapy with surgery, or chemotherapy and radiation therapy with surgery) is still under clinical assessment. Recent randomised control trials have shown that combining surgery with pre-operative chemotherapy can improve rates of 5-year survival in patients with locally resectable adenocarcinoma of the oesophagus, gastroesophageal Junction and stomach [104, 105]

At the time of diagnosis, around 30% to 50% of gastric cancers and 50% to 80% of oesophageal cancers patients have advanced disease and do not survive more than

a few months.[100] Hence, well developed palliative therapy is crucial, not only to offer symptom control, particularly for dysphagia, but also to provide a better quality of life for patients and their families by providing psychological and social support [10, 100].

Palliative treatment methods include endoscopic dilatation, stenting, contacts thermal therapy, laser therapy, argon plasma coagulation, Cytotoxic injection therapy, and Photodynamic therapy.[99, 100] Other standard non-endoscopic palliative options may include radiotherapy as well as chemotherapy.[100] Additionally, pain control, proper nutritional and psychological supports are equally as effective as the other palliative intervention mentioned [2, 10, 100, 106].

All these palliative options are complementary and may be used individually or collectively, as required. However, no evidence has been identified to confirm the relative effectiveness or appropriateness of these methods [10, 106, 107].

1.2 Upper GI cancer control strategies and service organization in England

Differences in survival rates in the UK compared with other European counties, as noted above, have prompted and guided recent cancer control strategies in England [24]. While the NHS Cancer Plan was published by the Department of Health in 2000 [108], its roots are in the integrated structure of cancer services in England and Wales, introduced by the Calman Hine report in the 1990s.[109] This reflects the government's ongoing strategy to combat cancer as one of its key health priorities:

"The government responded in the 1999 White Paper Saving Lives: Our healthier nation (Department of Health 1999), which focused on the four big killers, one of which was cancer. It pledged to reduce the death rate from cancer in people under 75 by at least a fifth (compared with 1996) by 2010, saving 100,000 lives."
Rebecca Rosen, Alex Smith and Anthony Harrison (2006)[110]

The NHS Cancer Plan was designed to enable early recognition of the signs and symptoms of cancer, with a strong emphasis on screening and on improved treatment options.[108] In addition, key targets including reducing the waiting times both for referral to diagnosis (most importantly the introduction of the Two Week Wait system "TWW"), and from diagnosis to treatment.[108] There is a further intention to invest more heavily in staff, facilities and in the strengthening and extension of high quality clinical research in this area. [10, 108]

In 2001, the UK National Cancer Guidance Steering Group created the ***'Improving Outcomes Guidance'*** for upper GI cancer management services.[10] Recommendations include the implementation of various routes of diagnosis for

patients presenting to general practitioners (GPs) with symptoms suggestive of OG cancer (Alarm symptoms).[10]

In addition, this national guidance service recommends the establishment of a well-linked clinical team from different specialties, hospitals and professional backgrounds, collaborating at the secondary care level as a coordinated multi-disciplinary team (MDT). Similar teams operating within the same region form a **Cancer Network**.[10] There are currently 30 networks in England **(Figure 1.3).**

These networks have been established to provide proper levels of expertise at various stages of care, such as curative surgical treatment and specialist radiology, oncology and palliative services to all patients living within each distinct geographical area [10, 111].

This text box is where the unabridged thesis included the following third party copyrighted material:

Clinical Effectiveness Unit, The Royal College of Surgeons of England, The Association of Upper GI Surgeons (AUGIS), The British Society of Gastroenterology (BSG), The NHS Information Centre for health and social care. National Oesophago-Gastric Cancer Audit: An audit of the care received by people with Oesophago-Gastric Cancer in England and Wales 2009, BSG.

Figure 1.3 The 30 cancer network which has been published by the National Oesophago-Gastric Cancer Audit 2009.[16]

The National Guidance Steering Group also recommends appointing a lead clinician for each team within a Network, and that this clinician should oversee the production of approved assessment and referral strategies, specifying the type and sequence of diagnostic and staging facilities to be used across the Network, based on up-to-date evidence and clinical guidelines. This is aimed at preventing unnecessary repetition of testing, as well as reducing delays in diagnosis. Furthermore, every MDT needs to avoid unbeneficial intervention, partly through the careful selection of patients with an early stage disease suitable for radical treatment (which could perhaps offer the possibility of long term survival).

Although there is no clear evidence to support which palliative treatment options should be applied, nevertheless it is highly recommended that a local arrangement within the each network should ensure the availability and efficient use of such palliative procedures as are necessary to improve the patients' quality of life. [10]

The quality of care given to these cancer patients have recently been examined by the national OG cancer audit programme.[112-114] This audit mainly describes the organization and process of care, as well as the outcomes of both curative and palliative treatment, thereby helping secondary services to improve.[112-114]

Since the introduction of urgent referral pathways for suspected cancer by the NHS Cancer Plan (2000) which was further supported by NICE clinical guidelines for urgent referral (2005),[115] the Cancer Reform Strategy (2007) has identified early cancer diagnosis as the key to improving cancer outcomes in England.[116] The National Awareness and Early Diagnosis Initiative (NAEDI).[116-118] was also launched in 2008, and it currently represents the partnership between the National Cancer Action Team, the Department of Health, and Cancer Research UK.[116-118]

NAEDI promotes four major work stream activities which constitute the framework for the 'NAEDI pathway' (Figure 1.4). [117, 118] The first work stream involves improving public awareness of common signs and symptoms of cancer. For example, the Doncaster Cough Campaign run by the North Trent Cancer Network has led to an 8% increase in the percentage of patients diagnosed at an earlier stage of lung cancer as a result of the following simple but informative statement: *"Cough not better after three weeks? Better go to your doctors now"* which causes

an improvement in the number of individuals consulting their general practitioner at an early stage, thus leading to a greater likelihood of earlier diagnosis.[119-121]

The second work stream is aimed at overcoming the clinical and system interface between primary and secondary care, and better determining the commissioning and gatekeeper role of primary care.[117, 118] With around £250 million announced by the Department of Health, the third work stream focuses on improving GPs access to key diagnostic investigations such as chest x-rays, non-obstetric ultrasound scan, MRI, and Flexi sigmoidoscopy/colonoscopy aiming to improve the chances of earlier diagnosis of lung, ovarian, brain and colorectal cancers respectively.[117, 118] The fourth work stream is intended to evaluate, inform and support effective NAEDI activity though high quality research investigation.[117, 118]

Figure 1.4 The National Awareness and Early Diagnosis Initiative (NAEDI) pathway.[118]

Guidance relating to the centralization of surgical resection is another important aspect of this implemented strategy,[122] since it has been demonstrated that there is a strong relation between the mortality rates of oesophageal and gastric cancer surgery and the volume of these operations performed by a specialist surgical centre [100, 123-126]. Recent evidence of lower short-term and longer-term mortality for patients resected in high-volume centres has been published by the National Cancer Intelligent Network (NCIN) group, further supporting the call for greater centralisation of oesophageal and gastric cancer surgical services in England.[127]

In 2011, the government strategy *Improving Outcomes: A Strategy for Cancer* (IOSC) was developed to tackle the possible inequalities, both in terms of experience of care and in outcomes of cancer among the UK population.[120, 121] IOSC further supports the above initiatives and sets out the ambitious target that by 2014- 2015 around 5000 lives per annum could be saved, which would bring survival in England up to the average for Europe.[120, 121]

Recently, the Operating Framework for the NHS 2012/13 has added further strength to IOSC by affirming that patients should have appropriate access to diagnosis and treatment.[128] It also provides patients with a right to be examined by specialist within two weeks from urgent GP referral where cancer is suspected. There is an expectation by this Operating Framework that less than 1% of patients should not wait longer than six weeks for a diagnostic investigation.[128]However, the likelihood that this waiting target can be achieved within primary care has not

been evaluated specially for patients with a suspected OG cancers where there is a predictable variation in the interpretation of dyspepsia guidelines.

Summary box 3

The rationale, main components and ambition of the national cancer plan, cancer reform strategy, NAEDI and the IOSC have been described. – At the time of commencing this research, there is a lack of evidence to suggest significant improvements in outcomes have been achieved for OG cancers in England. A national audit programme has described variation and trends in aspects of organisation, process and outcome for OG Cancer [112, 113], but its emphasis has been mainly on auditing specialist hospital care and pathways after cancer diagnosis. Less attention has focused on the earliest stages of the diagnostic pathway, in particular the likelihood that legitimate variation exists within primary care in relation to interpretation of existing dyspepsia guidelines, thresholds for referral and hence rates of diagnostic gastroscopy activity within practice populations.

1.3 Gastroscopy procedure

A gastroscopy is a procedure that uses a thin, flexible tube called an endoscope to visualize the oesophagus, stomach, and duodenum; hence it is called Upper GI endoscopy. This procedure is also commonly described as a Camera test because it has a light and a camera which are used to send images of the upper GI tract to a television monitor.

Gastroscopy is a very common outpatient procedure, generally performed to investigate dyspepsia. It has been estimated that around 1% of the population of England annually undertook an upper GI endoscopy.[129] This type of procedure not only provides direct visualization that can detect Ulcers, abnormal growths, precancerous conditions, inflammation and hiatal hernia; it can also be used to biopsy tissue, to remove stuck bits and pieces such as food, and to treat conditions such as bleeding ulcers or varices.[1]

Although upper GI endoscopy is widely considered to be a very safe medical procedure, there are some who argue that the procedure still carries a small risk of serious complications.[130] Potential risks of diagnostic gastroscopy include abnormal response to sedations (e.g stroke), infection, bleeding, and accidental tearing or perforation of the upper GI passages.[130-132] In England, the chance of such adverse effects has been estimated at 1 in 1,000 cases. [131] Data also suggest that 1 out of 25,000 cases may suffer a stroke related to the sedative effects of the procedure.[131] less serious complications such as sore throat happen in up to 10% of the patients.[133]

In the UK, it is only since the 1960s that a small number of gastroenterologists have been able to make use of the first commercial flexible fibrescopes.[134] However, the modern era of this procedure began in 1970s with the submission of Klaus Schiller's ***"Memorandum on Future National Needs for Fibre-Optic Endoscopy of the Gastrointestinal Tract"*** to the Department of Health [135]. The document laid out the case for much more serious investment in resources in this area (Schiller, 1973):

"It is no longer acceptable to do what is possible with available resources, but necessary to press for the facilities, equipment and staff to do what should be done... What started as a part-time hobby in the early days became a serious service commitment. The toys became tools, and then taskmasters." British Society for Digestive Endoscopy [135]

One of the most important health service measures linked to this procedure in 1970s was the initiative of providing general practitioners with free access to gastroscopy services.[136] Although at that time many endoscopy units were reserved for specialist use, various studies provided evidence that the introduction of open access gastroscopy (OAG) would not increase the number of "unnecessary" examinations, particularly for patients over the age of 50 years, and confirmed on the contrary its potential for reducing the burden on hospital outpatient departments. Such findings and recommendations led to its much wider availability. [136-142]

In 1991 the British Society of Gastroenterology (BSG) stated that OAG to general practitioners should be offered by all endoscopy units.[143] This publication also described the endoscopic workload in various part of the country and dealt with the developmental needs and likely expansion required in terms of the professional

training, equipment and staffing necessary for purposely built endoscopy units. [143] By1994, the second BSG survey of endoscopy practice confirmed that the above provision of OAG in the UK had increased to 74%, and that most endoscopy units were offering true OAG within agreed guidelines and protocols.[142]

Also in 1994, under the support of the Academy of Medical Royal Colleges, the Joint Advisory Group on Gastrointestinal Endoscopy (JAG) was established [144], with the objectives of setting standards for endoscopists, as well as providing UK wide support for endoscopic services, to make sure that practitioners would have the appropriate training and skills to carry out effective endoscopy.[144] JAG also aims to offer consultancy assistance to endoscopy units relating to their structure, resources, management, motivation, operations and the improvements necessary for providing high quality, patient-centred endoscopy services.[144]

Within the same year, the role of nurse endoscopists was widely established, as it was shown that independent practitioners throughout the UK were making a major contribution to endoscopic services. [79, 145]

Nearly ten years later (2001), the Endoscopy Committee within the BSG reported its updated **"*Provision of Endoscopy Related Services in District General Hospitals*".** This document highlighted the national increases within the requirements for gastroscopy which was estimated at a rate of as high as 15 gastroscopies per 1000 population per year.[146] As a result of such high demand for this procedure, the society further recommended the wider spread of Open Access Services, Primary Care Based Endoscopy units and an increased role for Nurse Endoscopists.[146]

More recently, the National Institute for Health and Care Excellence (NICE) set up the referral criteria for upper GI endoscopy, classifying any referral as being in need of **Immediate referral**; of **Urgent referral**; and **Non-urgent referral**. Although these criteria were based mainly on recommendations and guidelines for managing dyspepsia in primary care [147], when take in conjunction with the guidance on referral for suspected upper GI cancer [148], it was regarded by NICE as a crucial first step in managing the flow of patients for endoscopy.[149]

Summary box 4

Gastroscopy is the gold standard test for evaluating the upper GI tract. Although generally safe, like any invasive medical intervention it is associated with patient inconvenience, discomfort and a finite risk of adverse complications. In the UK the idea of wide spread availability of diagnostic gastroscopy procedures has been developed over the last four decades. Direct access gastroscopy services have been implemented, evaluated and quality assured across the NHS and made available to primary care clinicians. The high prevalence of dyspeptic symptoms means that potential demand for such services is very high with major cost implications. The next section describes how guidelines have sought to rationalise the use of gastroscopy based on the low yield of serious disease, the availability of effective empirical treatments and the option of less invasive investigational strategies.

1.4 Suspected OG cancer management and referral pathways in England: a primary care perspective

The cancer diagnostic process for general practice represents a complex area of clinical activity. For example, some cancers such as those of the oesophagus or stomach are relatively uncommon conditions, rarely encountered by a typical general practitioner, whereas the core symptoms of this cancer as described earlier (dyspepsia) are very common. Hence, diagnosis of malignancies with the high degree of overlap in symptoms for serious and common benign conditions represents a real challenge.

1.4.1 Dyspepsia clinical guidelines managements in primary care: when to refer for gastroscopy?

Dyspepsia is a common gastrointestinal complaints in general population. It has been shown that 25 to 40% of the population who experience this condition will consult their GP doctor. [37, 150-152] Even though the main causes for primary consultation remain unclear, some factors have been addressed, including the severity of the symptoms, low socio-economic class, older age and the fear that cancer may prove to be the serious underlining cause.[1] Nonetheless, less than 2% of dyspepsia patients referred for endoscopy are subsequently found to have OG cancer [2, 83]. It has been estimated that in the UK, dyspepsia has per year cost of approximately £1 billion. [153]

Given that dyspepsia has a major impact upon the patients' quality of life, and creates enormous costs for the community [154], guidelines for effective dyspepsia management have been drawn up and regularly revised **(Table 1.4)**. [37] Although,

clinical diagnosis remains relatively ineffective at distinguishing between organic and non-organic disease, with the detection rate of OG cancer remaining at only 1-3%, nevertheless patients with dyspepsia are still considered to be 'at risk'. [99, 155]

All recent guidelines strategies **(Table 1.4, Figure 1.4)** have centred around four main aspects; the definition of dyspepsia; when to refer patient for gastroscopy (the upper age limit for gastroscopy referral); the local prevalence of *H.pylori* (and the application of "Test and Treat" approach); and the use of empirical PPI.[37] However, none of the cost-benefit considerations supporting established guidance for dyspepsia have considered the case of non-referred patients – individuals who were considered to be at low risk but who were subsequently found to have cancer.

In spite of the differences in the methodology used, as well as in the backgrounds of the development groups and the target audiences, the guidelines present a remarkably consistent management approach for dyspepsia.[37] However, there is no clear evidence for the use of an upper age limit for gastroscopy referral, a notion which is associated with delayed diagnosis,[37] and any concern that cases of malignancy may be missed still does not justify automatic endoscopy in patients aged less than 55 with an uncomplicated dyspepsia.[156]

Initial diagnostic endoscopy in patient with dyspepsia who is under the age of 55 is still not recommended as it is considered as being not cost-effective and still there is not enough evidence that it does lead to improved outcome.[1]

In relation to cancer diagnosis *per se*, a more intensive strategy might seek to detect disease at an early stage either (a) by looking for cancer in all symptomatic dyspeptic subjects (without limiting prompt investigation to those with alarm features or non-response to initial empirical treatment); or (b) by "screening" symptomless individuals for early tumours. Such an approach is still not recommended in "low risk" western populations, since there is no clear evidence that mortality rates from OG cancer would be diminished.[1] However, "at risk" populations, such as those diagnosed with Barrett's oesophagus are often followed up through regular "surveillance" to identify pre-cancers (dysplasia) and/or early stage cancer (neoplasia), which it is hoped will provide significantly improved outcomes [1, 157, 158].

On the other hand, in parts of Asia, such as in Japan, where gastric cancer is known to be a major killer, it has been proven that mass X-ray, and more recently mass endoscopic screening methods, are useful in the detection of early stages of gastric cancer, and that such strategies subsequently reduce mortality rates. Tashiro et al. report that the latter method can be particularly effective if a sufficient number of skilled endoscopists are widely available. [2, 159]

Table 1.4 adapted from Ford and Moayyedi's 2008 summary of the guidelines for dyspepsia management according to their place of origin. [37]

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Ford, A.C. and P. Moayyedi, *Current guidelines for dyspepsia management.* Dig Dis, 2008. 26(3): p. 225-30.

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Ford, A.C. and P. Moayyedi, *Current guidelines for dyspepsia management.* Dig Dis, 2008. 26(3): p. 225-30.

Figure 1.5 Dyspepsia guidelines summary for the differences in the upper age limit for gastroscopy referral according to their place of origin adapted from Ford and Moayyedi's 2008 summary of the guidelines for dyspepsia management.[37]

Summary box 5

The potential demand for gastroscopy is large and European and North American guidelines have favoured initial empirical treatment and *H. pylori*-based 'test and treat' strategies over automatic investigation of dyspepsia unless there are obvious alarm features.

1.5 Delays in cancer diagnosis and the role of the "gatekeeper" approach

Distinguishing patients who can be managed within the GP practice setting from patients who need referral to specialist care is generally described as the gatekeeper role of primary care. [160] This role is considered a central aspect in the cancer diagnostic process, and yet it can also be a potential source of avoidable delay in cancer diagnosis within the NHS and in other countries with similar systems.[33]

It has also been cited that patients with lower-than-average outcomes may be a sign of inappropriate care pathways and/or may indicate that these patients have deteriorated more than should have been allowed by the inadequate provision of healthcare in primary care, or as outpatients in hospital. [161]

The biological nature of the disease means that it is unavoidable that some cases of cancer in general will not be diagnosed until the patient is admitted to hospital as an emergency case. There are also some cases which may be diagnosed through screening programmes. However, the vast majority of cancer cases are first presented, with signs and symptoms, to primary care. [162, 163]

Researchers have noted that late cancer diagnosis and its consequences cannot be attributed exclusively to the primary care initiation of an investigation of potentially cancer-related symptoms (so-called "doctor delay"), since this might also be assigned to other factors include the patient's late presentation ("patient delay"), or the referral process and variations in access to diagnostics ("system delay").

[164, 165] Nevertheless, primary care delay and system delay have been shown to account for the majority of delays within the UK system. [166]

This text box is where the unabridged thesis included the following third party copyrighted material:

Hansen, R.P., et al., *General practitioner characteristics and delay in cancer diagnosis. a population-based cohort study.* BMC family practice, 2011. 12: p. 100.

Figure 1.6 shows the various level of delay within cancer patients diagnosis and care pathways, adapted from Hansen et al 2011. [167]

An ecological study investigating cancer survival rates in 19 European countries, in a comparison of their gate keeper systems found that the countries with a more restricted "strong" gatekeeping approach are associated with poorer cancer survival rates than those with a weak gatekeeping system.[168]

In Denmark, which has a comparable cancer-related poor outcome, with a similar health-care and gatekeeper system to that of the UK, shows patient and system delay accounting for the majority of the delay in cancer diagnosis.[169] On the other hand, the Netherlands and Australia, both of which operate a similar gatekeeper system, report much better cancer-associated outcomes. Hence, it has been proposed that these differences may be explained by the different levels of access to diagnostics available in otherwise similar healthcare systems.[170]

However, there is as yet no clear evidence available in the literature supporting the idea that the availability of open access endoscopy can be associated with improved survival. A study by Sunder et al. (2006) also suggests that simply by limiting open access gastroscopy to patients with alarm symptoms, a small number of patients with potentially curable disease might be missed.[171] Nevertheless, it was suggested that direct access endoscopy may not only reduce the time to cancer diagnosis, but may also provide potential psychological benefits to patients, as well as reducing the proportion of patients diagnosed in an emergency situation. [172, 173]

In the UK, despite the extensive investment that has been put into securing early diagnosis (in particular the establishment of the TWW for fast-track referral so that a specialist can see a suspected patient as quickly as possible, together with the supporting guidance from NICE), there has been little improvement in the detection of curable cancer. [164]

Even though the logical concept that fast-track assessment of suspected cancer cases by specialist within 2 weeks of GP referral is worthwhile, there was no robust supporting evidence before its application would suggest improve outcomes.[174, 175]

Overall, it has been shown that the TWW did not improve the processes of identifying patients at their earlier staging of the disease [176], and approximately three quarters of cases of oesophago-gastric cancer are still diagnosed at a late and inoperable stage.[33, 177]

Studies have also demonstrated that a quite significant amount of cancer diagnosis occurs outside the TWW system [173, 176, 178-180]. In addition, it has been argued that the TWW produces a two-tier service, with a considerable number of patients in the second tier who have not only missed the rapid diagnostic facility, but who also experience longer waiting times in the routine way. [181] This group of worse-off patients could perhaps be diagnosed though the emergency route.

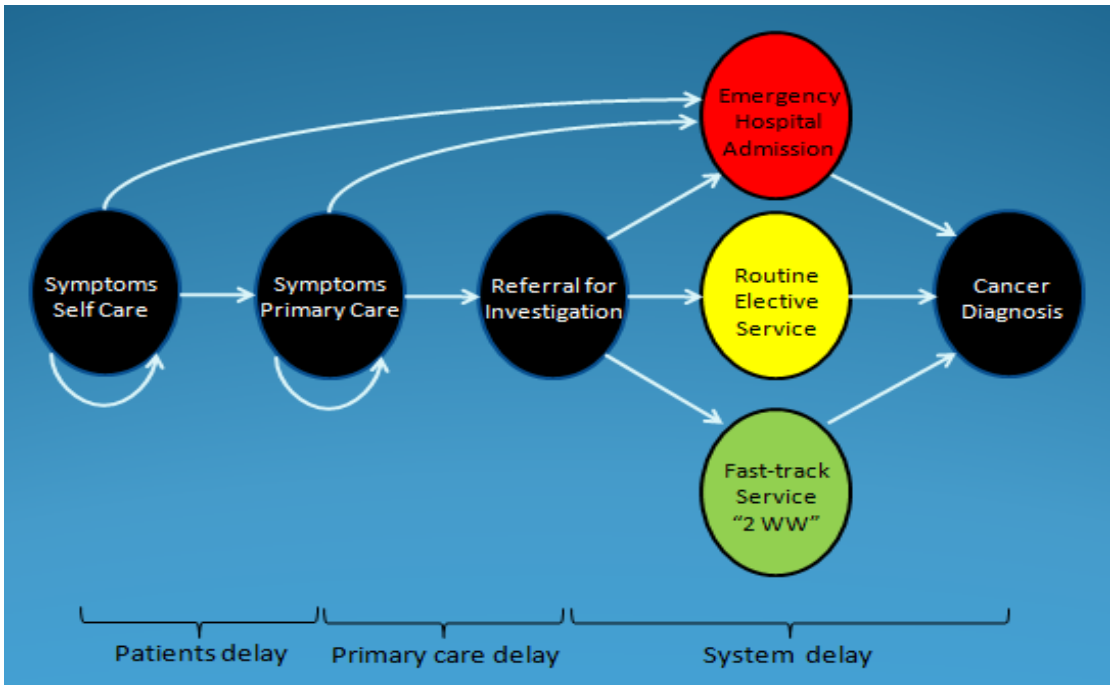

Figure 1.7 Cancer patients' pathway with various stages of care and route of diagnosis and managements.

Hanna et al (2005) conclude from a review of the relevant literature that the TWW is unsatisfactory on its own, and would not have a major effect on survival, since the delays caused by GPs represent simply a small portion of the 'cancer pathway' [173].

In 2011, the RCGP published the first English national audit of cancer diagnosis in primary care, in which 1170 GP practices participated, collecting a year's worth of data on 915 OG cancer patients (596 oesophageal and 319 gastric) from 20 cancer networks.[182] This audit examined the number of times patients present with possible symptoms of cancer before being referred for specialist opinion. The results show that 19.3% of oesophageal and 25.8% of gastric cancer patients had three or more consultations before referral, and that only around 58.2% of oesophageal and 40.4% of gastric cancer were referred through the two week urgent referral pathway.[182]

Summary box 6

Delayed cancer diagnosis is a real challenge. In the UK, GPs have access to the" Two Week Wait" system for urgent referrals and well established access to diagnostic gastroscopy. But, GPs serve a 'gate-keeper' role which is based on guidelines and referral criteria for dyspepsia that focus on 'alarm symptoms' as triggers for investigation. Current guidelines tend to encourage low rates of gastroscopy and endorse a 'watch and wait' approach.

Does adherence to the guidance contribute to most cancer cases being diagnosed at a late/incurable stage? If primary care were to adopt a lower threshold for gastroscopy, might that translate into better cancer outcomes?

1.6 Meaning and Explanation of variations in health care: differences in GP referral rates and health inequality.

Variation in health care and clinical activity is a widely distributed phenomenon within and between countries. There are sizable differences in terms of patients' access to health care and their disease related outcomes between patients when aggregated at the level of GP practices, primary care trusts, hospitals and regions.[183-186] Wennberg (2010) sees ***"unwarranted variation"*** as ***"variation in the utilization of health care services that cannot be explained by variation in patient illness or patient preferences."*** [186]

Clinical practice variation has been recognized in England and Wales since 1938, when a tenfold difference in the rate of tonsillectomy operation was reported.[187] Decades later, an increasing body of data has documented large differences in the utilization of health care services between different geographic areas, a finding which holds true in many countries, regardless of the diversity of the organisation, operation and funding of their health care system.[188-196]

Although healthcare managers, clinical researchers and physicians interpret variation differently, as they are pursuing different objectives,[197, 198] nevertheless variation remains of vital importance to individual patients, because at the personal level, the balance between good and bad depends not only on the evidence of the outcome of the intervention but also on the rate at which the intervention is accessible.[185]

It should be remembered that not all variation is necessarily bad or unwarranted, and that some is even desirable, because new and improved ways of patients' management could result from positive variation.[197] As Mulley (2010) points out:

"If all variation were bad, solutions would be easy. The difficulty is in reducing the bad variation, which reflects the limits of professional knowledge and failures in its application, while preserving the good variation that makes care patient centred. When we fail, we provide services to patients who don't need or wouldn't choose them while we withhold the same services from people who do or would, generally making far more costly errors of overuse than of underuse." *[199]*

However, the King's Fund Group (2011) notes that identifying what proportions of variation could be considered as *'good', or "warranted"* remains highly problematic: [200]

"*If variations represent evidence of inappropriate care, which care is inappropriate? Are the regions, or institutions, or practitioners with high rates over-providing, or are the low ones under-providing, or does the 'best' rate lie somewhere in the middle (or beyond either end)?"* *[200]*

Although some commentators argue that population dissimilarity, as well as data issue, might provide some explanation of this phenomenon, [186] a quite significant body of the literature concludes that variation is generally unexplainable and is often unavoidable because of the complexity and the unfeasibility of controlling of all the variables that may generate it.[200, 201]

Another explanation involves the notion that uncertainty about the effectiveness of health services and/or the level of intolerance of diagnostic uncertainty leads physicians to differing conclusions about when to perform various investigations or managements. [188] This hypothesis implies that while physicians may agree on

indications for procedures that are clearly appropriate, and on those that are clearly inappropriate, there nevertheless remains a large "grey area" in the middle, over which much disagreement exists.[188, 202]

Additionally, Chassin (1993) points out that geographical differences in health care could arise when large numbers of physicians in one area become more enthusiastic about a particular procedure or health related condition. [188] In this regard, Cummins (1981) notes that doctors tend to have unique 'referral thresholds' or referral habits which are not only affected by their level of training and experience, but also through their tolerance of uncertainty, personal enthusiasms and sense of independence.[203] However, this enthusiasm may also lead some to employ these services for inappropriate reasons.[188]

In 1948, the UK developed the National Health Service (NHS) on the basis of the clinical need for obtaining health care, regardless of whether a patient is able to pay for it. The NHS was described as a universal service, aiming at being **"*available to all irrespective of gender, race, disability, age, sexual orientation, religion or belief*"**. [204] However, variations in referral rates from generalists at the primary care level to their more specialised colleagues within the secondary care system remain a long-standing clinical and economic concern.[185, 186, 205, 206]

It has been demonstrated that this variation cannot be explained by dissimilarities in patient morbidity or by data error.[207] Moreover, only small percentages of variation can be accounted for in terms of differences between individual GPs. [205, 208] Even though the appropriateness of these referrals (particularly at the higher

level) has been questioned by many, this does not fully explain such variation.[208-211] On the contrary, there remains serious questions concerning inequity in access to specialist services, the effectiveness of primary care and the ineffective utilization of healthcare resources.[207, 208, 212]

In the UK, national clinical guidelines based on a mixture of evidence and expert agreement help GPs to decide which patients need to be referred to more specialist services for further investigation.[147, 148, 213] Although some studies have shown that these referral guidelines could be used to control the number of patients referred to hospitals, and might save costs and reduce unnecessary investigations [214, 215], nevertheless the recent NHS atlas of variation indicates widespread variation in GP referral rates, particularly for suspected cancer cases.[185] Additionally, Baughan et al (2011) have shown that many patients who fall outside the national guidelines were later diagnosed with malignancy, suggesting that there might be reasons other than those in the guidelines which might make GPs suspect the necessity for referral.[216]

Summary box 7

Uncertainty remains over the role of referral guidelines *per se* in achieving reductions in the wide variations observed in referral rates from primary to secondary care.[217] Current guidelines for investigating upper GI symptoms are controversial and lack a strong evidence base in terms of promoting optimal cancer outcomes. There is no current evidence to suggest that OG cancer patients belonging to practices at the lower end of the referral rate spectrum for gastroscopy experience any increased risk of poor outcome. The research described in this thesis seeks to apply epidemiological methods to study variations in gastroscopy rates within general practice populations and to test whether this variation is associated with OG cancer outcome. Generating robust evidence to link activity levels to outcome has potential to inform guidelines and policy.[218] At the level of primary care, a diagnostic pathway might be associated with a wide spectrum of rates of investigation between practices serving similar populations. However, without evidence for a link to differential patient outcomes there can be no understanding of whether low, average or high rates of referral are optimal for the condition of interest.

1.7 Evaluation of health care

In general, medical management aims to diagnose and treat diseases, to ease symptoms, to improve health-related quality of life and to save or prolong life. While wide variations in practice are perhaps inevitable, there is growing evidence that high rates of inappropriate healthcare, in terms both of the **type** and also the **time** of various medical interventions, can and should be avoided.[211, 219-223]

Anecdotally, health care providers or regulators (e.g. PCT, GP practices and hospitals) have shown concern about continued variations in the quality of care provided.[224-227] Providers' attention has also been directed toward a more evidence-based and cost effective approach to care provision.[228, 229] This in turn has led to an appreciation of the importance of using various performance and outcome indicators to measure the quality of care and service.[230]

Mainz (2003) provides a review of the definitions, characteristics, and categories of clinical indicators for quality improvement in health care internationally, noting that quality indicators are a necessary measure for helping identify the most appropriate course of action for a specific group of patients, or a health-related condition, ensuring that this is based on the most recent clinical guidance and/or evidence-based standards of care.[231]

One of the most comprehensive definitions within this review was developed by the Canadian Council on Health Services Accreditation (1996). This describes quality indicators as ***"measurement tools, screens, or flags that are used as guides to***

monitor, evaluate, and improve the quality of patient care, clinical support services, and organizational function that affect patient outcomes". *[232]*

Quality indicators can be rate-based sentinels that relate to structures, processes and/or outcomes.[219] They can also be either generic or disease specific. The structural element is the organisational framework, including the staff (e.g doctors and nurses), beds, equipment, and the other resources required to meet a defined standard of health care on a particular health issue; process refers to how such activities are delivered and used; and outcome refers to the effectiveness of these activities of interest (e.g. diagnostic procedures or interventions) in relation to patients' health. [219]

Table 1.5 Summarizing the most widely used characteristic for an ideal indicator. Adapted from **Mainz 2003**.[231]

Table 1.6 Examples of (A) indicators related to the structure, process and outcome of health care quality; (B) generic and disease specific indicators. Adapted from **Mainz 2003**. [231]

Despite the fact that performance indicators are considered a promising answer to the demands for improved quality within the health care system, still the evidence of these indicators' **value** in improving health outcomes of the population has been questioned in the literature. [228, 229, 233] For example; evidence about the effectiveness of Coronary Artery Bypass Graft (CABG), cataract surgery and of hip and knee replacement are well recognized attributable to health care, only if performed on appropriate patients. However, the ideal rates at which these procedures should be performed within the general population remains

unclear.[233] Similarly, an investigation of the use of waiting time data as a performance indicator in health care might offer easily measurable numbers, but this does not necessarily reflect the reality for the patients, the GPs, the treatment and/or the strategy behind these numbers.[234]

Therefore, careful development, interpretation and evaluation of quality indicators in order to study the relationship between the effectiveness as well as the efficient use of health services are necessary. Such evaluation is essentially based on the analysis of reliable and valid research data regarding the structure, process, and outcome of health care activities.[219]

Numerous research studies into a range of medical conditions (including congestive heart failure, stroke, and pneumonia) have shown significant linkages between processes of care and outcomes, particularly when the patient is the unit of analysis.[235] It is often necessary to evaluate the structure and process of care together, in order to interpret their outcome.[219] In other words, data concerning structure and process are fundamental if the researcher hopes to answer the question of whether the outcome of a particular disease was mainly influenced by the treatment itself, and/or as a result of the organisational framework (structure), or by the way it was delivered (process).[219, 236] For example; the patient's ultimate outcome for a coronary angioplasty could depend on where the procedure took place (organizational structure), or on whether it performed on the correct patient and on whether it was properly carried out (process).[236]

Fundholding is a crucial aspect to understanding the performance of any organization in seeking to create continuous improvement. Although research has

shown that differences in fundholding can explain only around 5% of the observed variation in referral, [201, 237] it is still logical to consider the effect of any commissioning process when evaluating health care quality. One of the essential aspects of these types of analysis involves identifying the best way to redirect resources toward those processes and structures of care that have been proved to have the most beneficial effect on patient outcomes.[235]

Value in health care is considered a common objective that should bring together the activities of all stakeholders. In this regard, Porter (2010) defines the concept of value in health care as *"the patient health outcomes achieved per dollar spent"*. He adds:

"Value should always be defined around the customer, and in a well-functioning health care system, the creation of value for patients should determine the rewards for all other actors in the system. Since value depends on results, not inputs, value in health care is measured by the outcomes achieved, not the volume of services delivered, and shifting focus from volume to value is a central challenge." [238]

It has also been shown that improvement in disease-related outcome is often associated with reduced costs; for instance, early detection of some medical conditions can lead to less complex care, and perhaps less invasive treatment with fewer complications, resulting in reduced need for subsequent follow up.[239] However, this hypothesis cannot necessarily be applied to the treatment of all diseases. Arguably, screening programmes that are directed towards a broad range of the patient population can result in decreased value.[239]

Summary box 8

Health indicators seek to measure organisation, structure, process or outcome of care in order to support quality assurance, allowing benchmarking between providers and analysis of time trends to monitor improvement. An increasing range of generic and disease-specific indicators are available and are used by central government, the department of health, commissioners and providers to measure NHS performance. Many indicators rely on analysis of routinely collected healthcare data, since prospective collection of bespoke audit datasets at the point of care delivery is logistically challenging, costly and often incomplete. The next section describes routine data in healthcare settings.

1.8 The use of routine health care activity data to drive clinical care and outcomes

Information continues to play an increasingly more central role in helping clinical staff to deliver safe and effective care to their patients. Many collected patient activity databases have been routinely developed throughout the world for the purposes of negotiation of hospital funding, allocation of resources, and strategy formulation within healthcare systems **(Table 1.7)** [240, 241]. Although most were never explicitly intended to be used for research purposes, recently they have been recognised as a unique data source for descriptive and comparative studies, and the number of specialist publications using these kinds of data sources is steadily increasing. [242]

When prospective randomised control trials cannot be conducted because of impracticalities, expense or for any other reasons, the use of large administrative databases can provide observational methods that offer the opportunity for the assessment of health care practice.[243] This can also establish a resource with sound external validity, which is sometimes hard to achieve in randomised studies.[243] Likewise, it allows measurements to be defined independent of specialist units participating in the prospective collection of clinical databases such as those used for local and national audits. Hence routine health care activity might permit improved analysis of real world outcomes.[242] Furthermore, many studies have shown the potential value of feedback and performance assessment with regard to health care providers. [214, 244]For these reasons, it is vital that we make the best use of the data sources available in our health systems.

Table 1.7 Summary of the various sources of routine data along with their strength and weakness. Adapted from Oxford hand book of Public health, by **Pencheon et al (2001)**.[245]

1.8.1 Hospital Episodes Statistics (HES) Data

1.8.1.1 The origin of HES data:

In England, the most inclusive and widespread source of information is the hospital activity data held in patient administration systems (**PAS**).[246-248] Information written by clinical staff in the notes, letters and/or discharge summaries are next extracted to the **PAS** by clinical coding staff who are responsible for the translation of diagnostic or procedural terms, as written by a clinician in the patient record,

into an alphanumeric code, using the International Statistical Classification of Diseases and Related Health Problems **ICD-10**, and the Office of Population, Censuses and Surveys Classification of Interventions and Procedures **OPCS-4**.[248] Subsequently, extracts from **PAS** are transferred to the Secondary Uses Service (**SUS**) which is the protected central data store that receives and processes patients' health related data for the whole of the NHS. After that, and at pre-arranged times during the year, **SUS** sends extracts to **(HES)** dataset **(Figure 1.7)**. [248]

HES is the England's storehouse for record level hospital data relating to all episodes of inpatient and day case care, and was originally started in 1987 following a report on the collection and usage of hospital information published by Dame Edith Körner (1921-2000).[246, 248] These data are available for each financial year from 1989-1990 onwards. Since its foundation, its data collection methods have changed substantially, mainly as a result to changes in NHS organisation.[246] For example, HES was first gathered (sub-nationally) by the regional health authorities, but in 1996 this process was moved to the NHS-Wide Clearing Service (NWCS). Since 2006, this has been taken over by the SUS, under the control of the Health and Social Care Information Centre and the National Programme for IT.[246, 248]

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rcplondon, *Hospital Activity Data A Guide for Clinicians, the RCP Information Laboratory (iLab) 2007*, Royal College of Physicians.

Figure 1.8 Information flows for routinely collected data from its starting point (patient notes) to its final destination (HES)[248]

1.8.1.2 Structure of HES data:

For each financial year (from 1st April to 31st March) there are millions of records (episodes of care) within the HES data storehouse. This information represents all NHS-funded admitted patient care, and private care within NHS hospitals in England [247]. An **episode** or **Finished Consultant Episode (FCE)** is the period of time a patient spends under the care and responsibility of one consultant team. This is different from the patient's entire stay in hospital (**Inpatient spell**) which may consist of one or more FCEs. However, when the responsibility of a patient is transferred from one consultant to another within an **inpatient spell**, this is called a **Transfer of care** process.[248]

HESID is the identifier that is unique to each patient and his/her HES.[249] This ID is essential for linking together records (episodes) for a single patient [247-249]. Each HES record (episode of care) can include more than 50 variables of information, collected directly by hospital providers or derived by the HES team. The nature of

information collected in HES for each patient and in each episode of care is illustrated in **(Figure 1.8)**. These data contain information about (A) Patients' demographics, (B) Hospital level administrative details, (C) Care providers and (D) Mode of admission as well as coded diagnosis and procedures. Details of all these variables will be presented in the main method section **(Chapter 2)** and the supporting appendices **(Chapter 7)**. Here it is important to note that the usual approach for analysing HES data as described in the literature encompasses extracting only episodes or admissions according to the coded "primary diagnosis" **(DIAG01)**, and then undertaking analyses on these extracted episodes alone and using the secondary diagnosis to study the patients' related co-morbidity. [250-252] There are several limitation to this approach which will be discussed in **(Chapter 3)**.

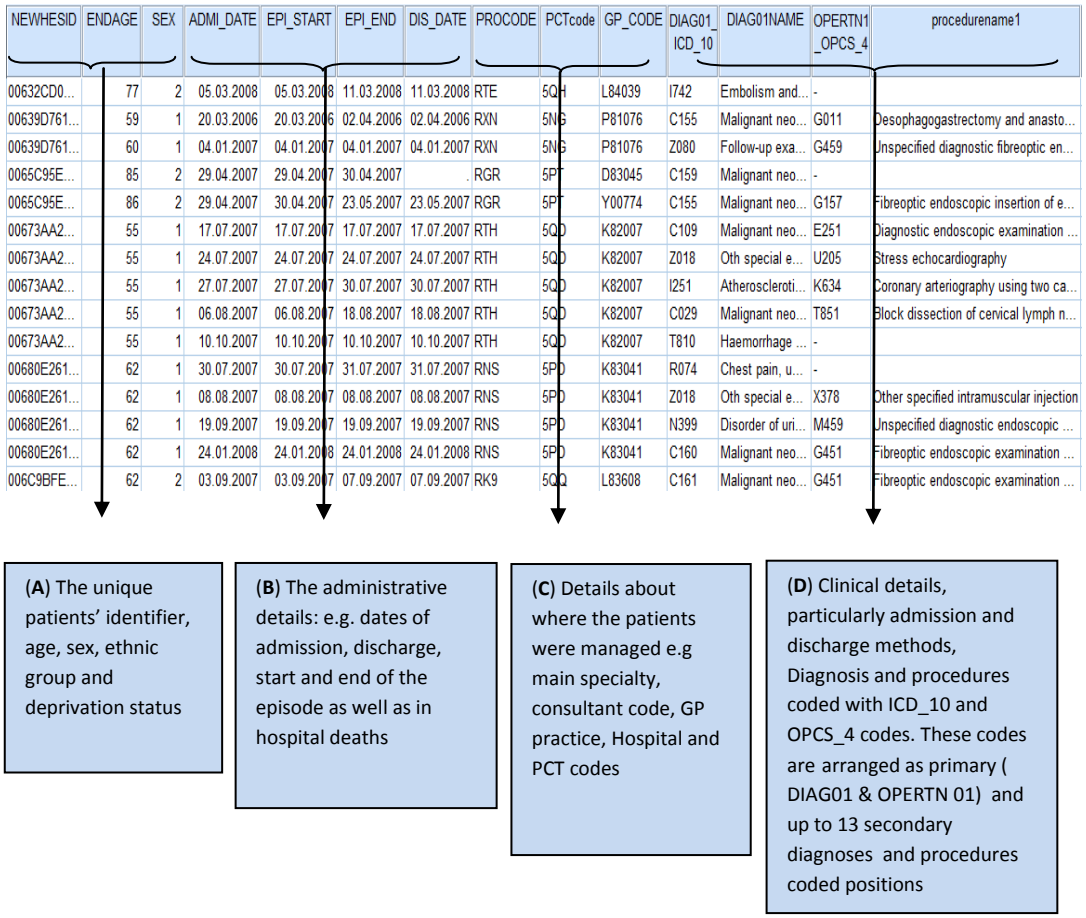


Figure 1.9 Illustrates the appearance of a typical extract of HES data. This data contains information about (**A**) Patients' demographics, (**B**) Hospital level administrative details, (**C**) Care providers and (**D**) Mode of admission as well as Coded diagnosis and procedures.

1.8.1.3 Limitations to the quality of HES data.

There is an anecdotal concern about whether these large datasets, which are intended for use in health service planning and financial management, can also be used to reflect clinical performance [253], or for auditing purposes [254], or to support the appraisal and revalidation of consultant physicians [255].

Additionally, it is believed by some that, such huge volumes of patient activity are generated continuously, and examination of every episode of care is not possible [248]. Furthermore, HES lacks information related to cancer staging as well as direct

information on the patients' quality of life or experience [247, 256]. Outpatient HES are still less complete and reliable; and fewer secondary diagnosis, co-morbidities and complications are recorded in the UK than are recorded in North America [241, 247].

The Royal College of Physicians (RCP) Information Laboratory (*i*Lab) notes that clinical coding rules and conventions are complex, and that accurate coding depends on clear medical documentation of diagnoses and procedures, as well as on effective translation of this information into codes by the coding staff. [257]

The RCT (*i*Lab) team also states that it is the responsibility of all NHS staff to guarantee that the information used in assessment making is as truthful and accurate as possible, since high quality information is essential for patient care, both directly and indirectly. Subsequently, *i*Lab has proposed various scientific methods and communication channels between clinicians and coding staff, with a view to improving the quality of the collected data **(Figure 1.9).** [248, 258]

In this regard, Williams and Mann comment that:

"Even if patient episodes are captured, the clinical data recorded may be inaccurate. A retrospective audit in two hospitals, comparing diagnosis codes assigned by local staff with those assigned by members of an external coding team who did not know the locally assigned codes, found exact agreement for the main diagnosis in 43% and 60% of cases, and approximate agreement in 55% and 72% of cases, respectively, in the two hospitals" [241]

On the other hand, Paul Aylin et al contest this finding, arguing that

"Problems with data quality are often not uniform but vary by coding field, clinical area, Trust or occasionally region and by year. The approximate agreements in diagnostic coding in one study were quoted as 55% and 72% in two hospitals for a random assortment of diagnoses, but the paper goes on to document agreements of 86% and 91% for specific diagnoses such as asthma."[259]

Moreover, Aylin adds that comparison of UK records of co-morbidities with those in the US is inappropriate, since placing the patient in a more significant diagnosis and management position might lead to the repayment of more health care costs, according to the US health care system [259].

Before making HES information available in the data warehouse, HES must be subject to various validation and cleaning stages.[246, 260] For example; a process called ***'autocleaning'*** ensures that data fields are inter-related and understandable both in isolation and also with reference to other variables. A subsequent process known as **'validation'** involves the testing of data against a set of rules to identify any problems that remain after the autocleaning process.[260, 261]

HES Processing Cycle and "autocleaning" are considered essential steps in data validation and cleaning to ensure and maintain good data quality. There is evidence that the coding accuracy of HES data has improved significantly over time. [262] Galland et al. (2000) found that HES coding for varicose vein surgery was 45% more accurate than local audit data in 1989, which had improved to 98% by 1995. [263]

In addition, a systematic review of twelve studies from England and Wales, plus a further nine from Scotland, analysed the use of HES, PEDW (Patient Episodes Database of Wales) and ISD-NHSS (Information and Services Division of NHS

Scotland), concluding that the coding accuracy in England and Wales is as high as 91% median coding accuracy for diagnostic codes, while in Scotland it is even higher, with 98% for procedure coding accuracy [264].

More specifically, the National Cancer Intelligent Network (NCIN) recently published its findings that only a small percentage of patients with oesophageal (0.7%) and gastric (0.3%) cancers were recorded only in HES, without documentation in the cancer registry over the ten years of the verification period (1998-2007) for data quality.[265]

Figure 1.10 Suggested ways to improve data quality. **RCP 2007**[248]

Summary box 9

Many studies have illustrated the potential contribution that the national HES data might make to understand care delivery and outcomes. But they also show how careful one must be to select the right cases for study and to use clinical knowledge in constructing analyses. It is the clinicians who understand the potential significance of the variables within the data, and can relate them to both local policies of care and to the terminology used in guideline documents. Thus, if this project can derive a subset of all individual patient episodes of care from a national cohort of patients with OG cancer from the HES data, it should, with a meaningful approach and analysis, be possible to track those patients along their care pathway and link unsuspected variations in a particular aspect of care to outcome.

Chapter (2) Rationale, Hypothesis, Aims and Methods

2.1 Rationale of the study

Over the last few decades oesophago-gastric malignant tumours have remained a worldwide challenge with little sign of major improvements in survival rates. Symptoms that might be an indication of early-stage OG cancer are very common and non-specific. Diagnosis therefore necessitates the investigation of symptoms though upper GI endoscopy (gastroscopy) in a relatively large group of patients, most of whom do not have malignant disease. OG cancer management involves complex decisions including the use of a relatively invasive endoscopic, surgical and oncological (non-surgical) approach. Cure is possible for a minority of cases through radical surgery and/or oncological treatment, but for many patients the disease is incurable at the time of diagnosis and the aim is to palliate symptoms.

Although epidemiological and socio-economic factors are likely to account for geographical variation in the outcome of this disease, there is concern that variation in practice and inequality in access to cancer services may play a role. Direct access to gastroscopy from primary care was established in England during the 1980s [142] and fast-track access for those with more specific alarm (or "red flag") symptoms was introduced into the NHS under the national cancer plan and the two week role system.[108] However, there has been little improvement in detection of curable cancer during this period.

There has to date been no assessment of access to investigation (gastroscopy) in relation to to OG cancer related outcomes. Furthermore, it is still unknown whether worse patient outcomes are associated with low levels of utilisation of this gold

standard diagnostic investigation technique, or conversely whether high levels achieve tangible benefits.

The NHS routinely collects a wide range of data about patients' demographic, clinical and administrative information, as well as details of where they were treated. Although this large source of information is regularly collected for analysis centrally, It has been argued that such analyses fail to explore the reliability and clinical relevance of the data and make ill-judged links to care quality.[241, 248] Hence, better techniques are needed to generate clinically-useful measures of care outcome capable of validation.

2.2 Hypothesis:

Outcomes for OG cancer may be associated with per capita rates of gastroscopy in the local general practice population. Specifically, cancer patients belonging to general practices with low rates of gastroscopy may have the poorest chance of a good outcome.

2.3 Aims and Objectives:

1. Using Hospital Episodes Statistics (HES) data, to develop and validate methods for identifying patient populations with a coding sequence of diagnoses and procedures compatible with incident cases of OG cancer. To check the face-validity of data outputs by reference to external sources (local audit data and published national statistics) and thereby confirm their suitability as a tool for studying factors associated with OG cancer outcome.

2. To analyse HES data, with linkage to external sources of population information at the general practice level, in order to explore variation of gastroscopy rates in the primary health care setting and then to test whether the gastroscopy rate in general practice populations in England is associated with patient outcomes for OG cancer.

3. To identify whether practices with 'low' gastroscopy rates appear to be operating more selective referral practice, as reflected in a higher yield of serious pathology among subjects referred for investigation. Methods will be developed to describe the diagnostic profile of all patients undergoing elective gastroscopy and to compare profiles across the spectrum of practices, both nationally (using HES data) and locally (using routinely collected endoscopy reporting data).

These elements constitute the three inter-related work streams that form the basic structure of this thesis. The findings of each element will be presented in a separate chapter, with its own background, aims, results and discussion section. The present chapter describes the various methodologies developed for data extraction,

internal and external linkage, case definition and specifications for the generation of patient-level variables, with reference to the relevant **Appendices** and **Syntaxes** (containing the listings used for code selection and syntax for data processing).

2.4 Methods:

2.4.1 Source and storage of Hospital Episode Statistics data

An extract of Hospital Episodes Statistics data for the years 2006-07 and 2007-08 were supplied by Northgate Information Systems as [**comma-separated values** or **character-separated values** (**CSV**)] files, which were imported into the statistical software package, SPSS (Version 18 and 20). The data were stored on the University of Liverpool server as SPSS data files. The electronic storage has restricted password-controlled access and is compliant with the data governance requirements for hosting and analysing HES data. The processing and analysis of HES data was undertaken mainly in the statistical software package (SPSS), although some steps required importing/exporting between SPSS and a spreadsheet package (Microsoft Excel) unless otherwise stated.

2.4.2 Extraction of valid episodes of care under adult medical and surgical specialties

This section focuses on a number of stages of data cleaning and extraction required for reducing the main HES dataset, to contain only care episodes of interest for assessing the coded OG cancer patient journey.

The original HES data contains episodes of care at acute NHS general hospitals and in other providers, such as paediatric hospitals or specialist maternity units. Initial data clean-up and filtering was undertaken for each individual data year followed by subsequent merging of the two data years. The procedures applied for the 2007-08 dataset are described in detail.

Episodes of care admitted under the main **medical** and **surgical** specialties were first extracted from the original HES dataset. This excludes specialities that are not relevant to the present study (such as gynaecology). This procedure relies on the **(Mainspef)** variable in HES, a variable that codes the specialty of the admitting consultant team. The list of codes included and the **syntax** used for selecting these care episodes is given in **(appendix 1**, **syntax 1).**

Further data clean-up was undertaken using the **ENDAGE** variable (patient age) in order to remove paediatric admissions (under the age of 16 years) and to remove episodes where there were missing or invalid ages (blanks or erroneous multi-digit values). The dataset was then limited to the 151 acute hospital Trusts in England **(Syntax 2)** using the relevant acute provider trust codes (**PROCODE** variable; see **Appendix 2** for list of codes). Additional episodes were excluded from the dataset using the **ADMIMETH** variable in order to exclude maternity-related episodes (31=Admitted ante-partum; 32=Admitted post-partum; 82=the birth of a baby in this Health Care Provider; 83=Baby born outside the Health Care Provider except when born at home as intended; 84 and 99=Unknown).

2.4.3 Identification of OG cancer cases and extraction of their comprehensive care histories:

A number of procedures for processing the data were designed, tested and implemented within SPSS in order to identify patients who had a coded diagnosis of oesophageal or gastric cancer at **any** diagnostic position and at any time within the available dataset. Once individual cancer patients were identified, all episodes of inpatient care for that patient were identified, extracted and ordered

chronologically in order to compile a complete record of all hospital care for each case.

The first stage of this process involves generating a list of all relevant diagnostic codes for OG cancer from the available International Classification of Diseases codes (ICD-10 version). The codes selected are given in **(Appendix 3)**. SPSS Syntax **(Syntax 3)** was written to flag the occurrence of any of these codes, not only at the primary position **(DIAG1)**, but also at any of the 13 other available diagnostic positions for each care episode (**DIAG2** to **DIAG14**). This generated a new binary variable (**OGCANCER**, 1=Episode contains an OG cancer code). Episodes with this variable (OGCANCER=1) were extracted, sorted by unique patient identifier (**HESID**) and by admission date in ascending order. Using the "identify duplicate cases" function in SPSS, the chronologically first episode of care containing a cancer code for each patient was flagged with a new variable (**PRIMARYFIRST**=1). These episodes were selected using the "selected cases" function and saved as a separate file. This file ("OGC cases") contains the first episode of care for each patient with an OG cancer code. Manual checks on a random sample of patients were completed to ensure that the syntax was identifying the correct codes in each diagnostic position.

Using the unique identifier for each cancer case, we then extracted all their care episodes from the main HES dataset. This involves identifying and extracting episodes where cancer was **NOT** a coded diagnosis for each cancer related HESID, by returning to the original dataset containing all care episodes under medical and surgical specialties ("Admitted Patient Care HES EPISODES dataset"). A new variable

(**IDENTIFIER**) was generated from the "OG cancer cases" file and the "merge" function in SPSS was used to flag all care episodes for the cancer patients; even episodes not coded with C15, C16 codes. These episodes were extracted and saved as a "MASTER FILE", one for 2006-07 and another for 2007-08 data year.

Most cases of OG cancer are diagnosed by gastroscopy. It is expected that some cancer patients' gastroscopy-related episodes might be coded with other diagnosis codes (such as "oesophageal stricture" or "gastric ulcer") without any cancer codes appearing in that episode. If a cancer code appears at the subsequent care episode when, for instance, the patient is readmitted for treatment of the cancer, then we know that the original endoscopy procedure was the point at which the cancer was diagnosed and the patient's "journey" began. This highlights the need to identify sub-groups of cases for analysis according to whether the HES dataset contains a related care information (preferably starting with a diagnostic procedure) or has missing elements suggesting missing information (e.g. coding problems) or a previously diagnosed "**prevalent**" case whose care had begun in an earlier year.

For these reasons, additional variables to act as a filter were flagged to show whether or not each patient had gastroscopy procedure highly related to the management of OG cancer within their episodes history. Such a filter was developed using published procedure codes and definitions.[266, 267] A syntax which includes these codes was then written up to mark these procedures **(Appendix 4, syntax 4).** Again this study was keen to show internal linkages, not only with procedures coded at primary position (**OPERTN 1**), but also at any other positions (**OPERTN 2** to **OPERTN 14**). Once the above syntaxes were processed,

(SPSS function: FILE > NEW > SYNTAX) a new field variable, called the **Gastroscopy filter,** was produced. This method was applied for both 0607 and 0708 OG cancer master dataset.

It also became essential to merge the 2006-07 and 2007-08 master data files for OG cancer patients. By do doing, we were able to trackback those patients who appeared in 2007-08 with no gastroscopy filter, to check whether the upper GI endoscopy code emerged in any episode relating to that particular patient within the 2006-07 data. To merge these two years' worth of OG cancer patients' history, it is important to make sure that all dataset variables are in the same order with the same variable names and format, and to have the same identifying HESID for each patient in both years before the merge. Additionally, prior to the merge, a new field was added to each master file called **YEAR,** to make it easier to identify which year the admission originated from. Afterwards, 2006-07 and 2007-08 master datasets were merged together to make a single dataset, again by using SPSS function (DATA > MERGE FILES > ADD CASES).

The newly merged file (2006-08 merged OG cancer patients' history file) contains all the episodes of care that are coded with oesophageal or gastric cancer (ICD-10 codes: C-15s or C-16s), in addition to other episodes which these patients had before and after the appearance of these codes between 1st April 2006 and 31st March 2008. As a result, it was possible to flag the key milestones, such as the first OG cancer and the first gastroscopy procedure coding dates in the patient's journey.

HES data does not include a date of diagnosis, and the first episode of care, coded with a definitive cancer code, is not a reliable starting point for the patient's journey.[268] Manual review of the coding sequence for individual cancer cases revealed that some of the original **primary diagnoses** recorded at the time of the first (index) gastroscopy were non-specific symptom codes (eg, dysphagia) or non-malignant diagnostic labels that would be compatible with cancer (eg, oesophageal stricture or gastric ulcer). The first appearance of a cancer code for such cases was typically within a few days or weeks of the index diagnostic gastroscopy, when the patient attended for another hospital episode (eg, therapeutic gastroscopy or surgery). By selecting cases whose first endoscopy episode occurred within 3 months of the first cancer-coding episode (either as a day-case or during hospital admission), we extracted a cohort of patients with a sequence of care episodes and procedures compatible with a new diagnosis of OG cancer **(Syntax 5)**.

2.4.4 Linkages of HES data to the statutory register of deaths data from the Office of National Statistics (ONS)

Death in hospital is a recorded variable in HES but the dataset does not capture deaths occurring post-discharge from hospital. The present project was able to benefit from having access to further linkage of HES data to the statutory register of deaths held by the Office of National Statistics (ONS), and by using the same SPSS function mentioned above, to link the death date for each patient as another variable within the merged two-year file. Consequently, the **DEATH DATE 0608** variable was created, comprising the death dates returned from death files 2006-

07/2007-08 ONS based on HESID. This new variable was used to give the number of cancer deaths and to enable crude mortality and survival analysis.

2.4.5 Patient factors: demographic, comorbidity and socioeconomic variables

Patients' age and gender are coded variables in HES. Patients' ethnicity groups were not available in the original 2007-08 data and hence this has not been included in this study. The recorded age of cancer cases was grouped into five year age bands (<55, 55–64, 65–74, 75–84 and ≥85 years) **(Syntax 6)**.

All diagnostic fields were screened for co-morbidities using ICD-10 codes from the Charlson index of co-morbidity [269, 270], in which OG cancer codes were omitted from the list **(Appendix 5 and 6, Syntax 7 and 8).** Every patient was assigned to the highest co-morbidity score within his/her coded care history within the dataset. A categorical co-morbidity variable was then allocated to each patient (none, 1 or ≥2 co-morbidities) as previously described using **(Syntax 9)**.[271]

Within HES data, each patient episode contains a deprivation variable for the socioeconomic status of the lower super output area of residence at the time of admission **(IMD04RK)**. Lower super output areas from the whole of the country (each including about 400 houses) were grouped into quintiles from the most deprived to the least deprived, based on their ranking in the Indices of Multiple Deprivation for England 2007.[272] Quintile 1 denotes patients living in the most socioeconomically disadvantaged areas of the country while Quintile 5 indicates the most affluent group **(Syntax 10).**

This ranking was originally made by combining the seven IMD domain scores using the following weights: [Income (22.5%); Employment (22.5%); Health Deprivation

and Disability (13.5%); Education, Skills and Training (13.5%); Barriers to Housing and Services (9.3%); Crime (9.3%); Living Environment (9.3%)].[273]

2.4.6 Patient outcome variables

2.4.6.1 Emergency admission during diagnostic pathway

Every hospital inpatient spell or daycase procedure mode of admission is either elective or emergency and is a recoded variable in inpatients HES records (Syntax 11). In this study, method for determining emergency presentations (diagnosis) of cancer cases are identified according to the episode containing the index (first) diagnostic procedure (gastroscopy) as either elective admission (i.e. daycase gastroscopy) or non-elective admission (i.e. gastroscopy performed during an unplanned 'emergency' hospitalization).

The present study aimed to use the most relevant clinical care event (i.e. the first gastroscopy procedure) to identify the point of diagnosis of OG cancer within inpatient HES data. More recently, Eliss-Brook et al used both inpatient and/or outpatient HES activity data to attempt to establish an elective or emergency route of cancer diagnosis for a range of cancer types.[274] Although Eliss-brook used the same selection of admission method codes for elective (codes 11, 12 and 13) and emergency (codes 21, 22, 23, 24 and 28) admissions as the present study, their methodology selected any inpatient or outpatient event in closest proximity to the date of diagnosis as determined by linkage to cancer registration records extracted from the National Cancer Data Repository.[274-276] However, this approach did not identify whether these events included a specific diagnostic procedure for the

cancer in question – thereby examining all-cause events rather that a defined clinical milestone in the patient journey.

The present study identifies an unplanned emergency diagnosis of cancer as representing the following categories of patient: (1) those admitted to hospital having never seen their GP and were diagnosed with cancer; (2) Patients who were very ill, or who had abnormal results, who had contacted their GP or the out of hours service, and were then admitted to hospital; and (3) patients who might be seen by their GP and were referred routinely or via a two-week wait, but who deteriorated before their scheduled appointment and were admitted to hospital and then diagnosed with cancer.

This defines the **mode of diagnosis** as either elective or emergency. Once the mode of ''diagnosis'' has been identified, it is re-linked according to HESID to be visible as the mode of diagnosis for every admission within the dataset, through use of the SPSS function DATA > MERGE FILES > ADD VARIABLES. It is important to note that any outcome measure used throughout this study (otherwise stated) has a value of 1 if the admission was emergency (unplanned), and 0 if not.

2.4.6.2 Surgery

Surgical intervention for oesophago-gastric cancer was defined on the basis of coding a major surgical resection compatible with curative intent, using a list of previously reported OPCS-4 codes **(Appendix 7** [277], **Syntax 12)**. Additional steps were undertaken to identify these surgical codes in specialist surgical centres (hospitals other than the 152 acute trusts). For example, major resections happen at the Cardiothoracic Centre-Liverpool NHS Trust (**RBQ**) includes cases which were

originally diagnosed at the Royal Liverpool and Broadgreen University Hospitals NHS Trust (**RQ6**). The identified surgical episodes through this procedure were then added to final analysis. Every cancer patient was classified as either having had a record of a major surgical resection or not. Where a patient might have a record of more than one OPCS surgical code allocated as a major resection for their treatment, these cases were only once in the analyses as they received a curative resection.

2.4.6.3 Mortality

The index diagnostic gastroscopy date was taken as the starting point or "provisional diagnosis date'' for survival analysis, and mortality rates were calculated at various post gastroscopy time points (e.g. 30 days, 6 months and one year mortality) using death dates linked from the Office of National Statistics. The SPSS function used to record the number of days in between these two landmarks was [TRANSFORM > DATE AND TIME WIZARD > CALCULATE WITH DATES AND TIMES > CALCULATE THE NO. OF TIME UNITS.] **(Syntax 13)**. It is important to note that patients with no death date were censored to the 31/03/2009, which was the last death (follow up) date coded among the ONS death data.

2.4.7 Gastroscopy procedures coded as in-patient or day-case procedure under adult medical and surgical specialties

Using the previously described two-year download of the HES dataset containing more than 24 million care episodes (2006/7 and 2007/8), all hospital episodes containing a procedure code for diagnostic gastroscopy for adult patients (≥16 years) were extracted using published procedure codes and definitions [266, 267]

(Appendix 4, **Syntax 4)**. The process of ensuring that no duplicate procedure is included within the extracted data was achieved by using SPSS function (DATA > Identify duplicate cases > Define matching cases by > HESID, Admission date, DIAG01, DIAG02, PROCEDURE1, PROCEDURE2, GPCODE, EPIEND "Episode end date" and Consultant code " CONSCD").

In England, all residents receiving NHS healthcare are registered with a general practice that comprises one or more family doctors providing primary care services to a defined practice population. Each general practice has an identifier code within HES. All gastroscopy procedures were recorded for persons registered at each general practice, via aggregate function within SPSS.

Published data are available for the total number of adult patients (≥16 years) registered at each general practice, their gender and age profile for the relevant years.[278-280] The average counts of elective gastroscopies performed per practice per year were calculated. This value was divided by the relevant practice adult population to give an annualised crude rate of gastroscopy. To ensure that differences in the number of events (e.g. gastroscopy rate) observed in two or more populations (GP practices) were not due to differences in the age and sex profile, data for the practice population demographic profile [278], was measured alongside the Indirect age and sex standardization (or adjustment) of rates [281].

Indirect standardisation method summary:

I. Calculate the number of OGD procedure related to every practice by 5 year age bands (15-19), (20-24),.....(80-84) and (>=85); and for males and females of the same age bands (15-19)m, (20-24)m,.....(80-84)m, (>=85), (15-19)f, (20-24)f,.....(80-84)f, and (>=85)f. These are the ''**observed events**''.
II. Calculate the **reference event** (total number of OGD procedures for the included practices) and **reference population** (total number of adult population registered in all practices in the study).
III. **reference crude rate** (OGD rate for England) = reference Event/reference Population*100,000
IV. Calculate the local (every practice) **expected events**= reference rate/practice population
V. The **standardization ratio**= the observed events / expected events.
VI. The **indirect age-sex standardized OGD rate**= standardized ratio*reference Crude rate/100.

2.4.8 General practice Index of Multiple Deprivation (IMD)

We assigned each general practice to a deprivation category (using deprivation quintiles of 1 = most deprived to 5 = least deprived). This was based on the national ranking of a practice-level average deprivation score based on the Index of Multiple Deprivation (IMD). The practice score represents a weighted average of the IMD scores for each Lower Super Output Area (LSOA) in which every given practice has patient registrations.[282]

2.4.9 Statistical analysis:

Analysis of variance and $\chi 2$ were used to compare differences in continuous and categorical variables. Univariate logistic regression was used to identify factors associated with emergency route of diagnosis, surgical resection rate and all-cause mortality at 1 year. Factors with a significance level of ≤ 0.1 on univariate analysis were included in the final multivariate regression model.

Chapter 3 Characteristics of the OG cancer patient population extracted from the Hospital Episode Statistics dataset, validation against independent national and local data and identification of patient-level predictor factors associated with cancer outcome

3.1 Introduction and objectives

Routinely collected information on patient care has become an increasing feature of the National Health Service [264]. Much of the analysis of routine data has been 'top-down' and clinical engagement in the generation, validation and use of analyses derived from these datasets has been limited.[248, 255, 257, 264, 283] There is considerable mistrust of data quality and a perceived lack of credibility for indicators derived from these routine statistics. [248]

The benefits of extending an audit beyond a local hospital or cancer network have increasingly been acknowledged [112, 113, 248, 254]. Although clinically designed and owned audit datasets are excellent ways for reviewing and monitoring current practice against a predefined standard, nevertheless this type of activity can be very expensive and time-consuming and is often associated with major concerns relating to its totality, case ascertainment and the lack of enthusiastic staff, and sometimes to inadequate financial and practical resources [112, 113, 248, 284, 285]. It is also noted that medical audits are frequently limited to common conditions or procedures.[248] Moreover, audit data collection is processed outside the route revealed in HES, and hence it lacks the routine internal quality checks (as might be provided by data quality meetings or clinical coding audits) that are essential steps in the cases of SUS and HES.[248, 255]

One example of such limitations was published by the Scottish Audit of Gastric and Oesophageal cancer 1997- 2000. Their report notes that:

"Approximately 60 % of the data were collected by the Data Mangers towards the end of the Audit because busy clinicians were unable to take the time to track down medical records and complete the forms. Therefore the Data Mangers faced lengthy searches for medical records, largely due to the fact that the locations of the medical records were inaccurately recorded but also because medical records had been destroyed following the patient's death in some instances. This has an impact on the completeness of the data collected on some patients, which resulted in some cases having to be removed from the database before the final analysis as the cancer could not be confirmed " [284].

On the other hand, there are legitimate and generic concerns regarding the completeness, precision and depth of routine administrative coding [264, 286, 287]. This chapter postulates that such issues with accuracy of diagnosis and procedure coding [286-288] are inevitable as the result of many factors. First, some diagnoses or procedures may be more difficult to code, for instance where the condition is rare and has a low prevalence or is difficult to diagnose. Secondly, there are occasions where the final diagnosis has not been finalised at the time of discharge, in which case coding of discharge data tends to be more prone to inaccuracy [250, 264, 289, 290].

In addition, the typical approach for analysing HES data as described in the literature involves extracting **only** episodes or admissions according to the coded "primary diagnosis", and then undertaking analyses on these extracted episodes alone, using the secondary diagnosis to study the associated co-morbidity [250-252, 291]. There are several limitations to this approach. Primarily, the coding of the main diagnosis may vary from one episode to the next, depending on the reason for admission. A range of conditions might appear as "primary" diagnosis at different times, particularly for a patient suffering from cancer.

The cancer code might appear as a secondary or lower order diagnosis, or may be missing entirely, from some care episodes. By applying clinical logic, knowledge of care pathways and creating linkages between consecutive episodes for individual patients, it could be possible to make better use of HES data.

In the case of OG cancer, the first care episode for a patient with an oesophageal stricture due to oesophageal cancer might be a daycase diagnostic procedure (Gastroscopy). This episode of care will be recorded in HES but the coded primary diagnosis may be "oesophageal stricture" and there may be no cancer code in any diagnostic position.

The results of biopsies taken during the daycase test may later prove that this stricture was cancerous. This would not be recorded in the original daycase episode in HES data, however. The patient may then have an outpatient visit and additional outpatient tests (e.g. CT scanning) but these are not recorded in the inpatient HES dataset. The next care episode appearing in HES data might be another daycase procedure, this time for palliative stenting of the tumour. This second inpatient episode is coded in HES with cancer as a primary diagnosis and with endoscopic stenting as a procedure. Two weeks later, the patient is admitted as an emergency to hospital with pneumonia, remains in hospital ten days receiving palliative care and dies. The coded primary diagnosis for this third and final care episode is "pneumonia" but a secondary diagnosis is recorded as oesophageal cancer.

A simplistic analysis of HES data using only episodes coded with a primary diagnosis of cancer would extract only the second episode of care from the dataset. However, once a case of cancer has been located in the dataset it should be possible to perform linkages in order to analyse all episodes of care for that patient, thereby identifying all relevant hospital interventions both *before* and *after* the first appearance of a cancer code in this patient's history.

3.2 Aims:

1. To identify cases of OG cancer with HES data and to extract all coded NHS care episodes for each patient, building up a chronological record of all inpatient episodes for each patient. This involves distinguishing patients with complete data pathways from those with incomplete pathways (prevalent cases from previous data year, or cases with missing care episodes).
2. To verify the accuracy of the flagged mode of admission ('emergency' versus 'elective') for the index care episode as derived from the above longitudinal internal linkage method in HES data. This involves comparing the flags derived from HES for a large sample of local cases (Aintree University Hospital, Liverpool, UK) with the 'true' (gold standard) mode of admission as determined from audit of the case records. Each local case extracted from HES will be linked to a verified local case on the basis of age, gender, GP practice and relevant episode dates.

3. To describe the demographic and basic clinical characteristics of cancer cases extracted for England (2006-2008), as identified through this methodology and compared with external sources of national data (e.g. prospective national audit data, and NCIN) – thereby establishing the face-validity of data outputs.
4. To study the association between patient characteristics such as age, sex, co-morbidity and deprivation and outcome of OG Cancer, thereby defining the case-mix factors required for adjusting outcomes for confounding in subsequent studies.

3.3 Method:

The main method used to extract patients population is described in **(Chapter 2)**. In summary, the number of stages of data cleaning was first required to reduce the main HES dataset, so that the data includes only care episodes of interest for assessing OG cancer patient journey. All patients with one or more episodes containing a diagnostic code for oesophageal or gastric cancer were first identified by looking at the cancer code, not only at primary position but also at every other diagnostic position within the data. Using the unique patient's identifier for each cancer case, we then extracted all their care episodes from the main HES dataset and ordered them chronologically.

Unlike the cancer registry data in which the date of diagnosis represents the date of the histopathology report (where available), HES data does not contain a specific date of diagnosis, and the first episode of care coded with a definitive cancer code is not a reliable starting point for the patient's journey.[268, 292, 293] The first appearance of a cancer code for such cases was typically within a few days or weeks of the index diagnostic gastroscopy when the patient attended for another hospital episode (e.g. therapeutic gastroscopy or surgery).

Government policy gives a target of 2 weeks between the date of referral and the date of diagnosis for urgent referrals from general practitioners and a limit of 62 day wait from urgent GP referral to first treatment for all cancers [108] OG cancer prospective (National) audit of cases collected within the same time window of this study shows that only 52% of urgent referrals were diagnosed within the target wait of two weeks. However, around 96.2% of these patients who were referred

through urgent GP referral pathway and 86.2% of patients referred through non-urgent pathway were diagnosed within 12 weeks. [113]

Hence, by selecting cases whose first upper GI endoscopy episode occurred within 3 months of the first cancer-coding episode (either as a day-case or during a hospital admission), we extracted a cohort of patients with a sequence of care episodes, and diagnostic procedures compatible with a new diagnosis of OG cancer **(Figure 3.1.)**. The successful development and validation of this complex linkage method was a key research milestone in the course of the project, since it was first necessary to overcome the limitations of HES data to extract a sample of OG cancer cases with strong face validity (i.e. total numbers, demographic profile and measured outcomes consistent with those expected for a national cohort of new cases).

Binary logistic regression was used to test whether there are associations between various patient-level factors, namely age; gender; co-morbidity and deprivation as a predictor of emergency admission at the time of diagnosis; chance of major surgical resection; and mortality at one year.

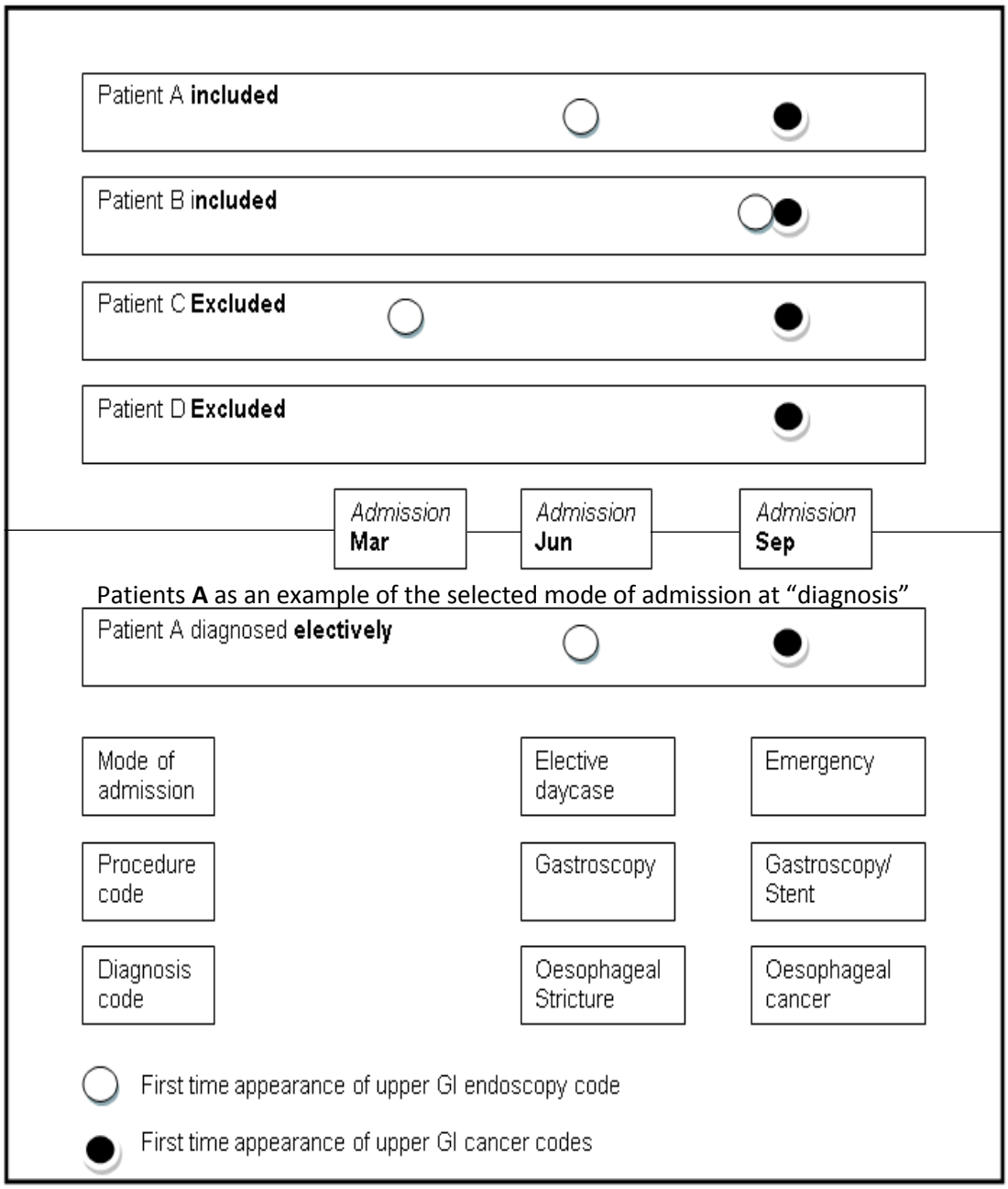


Figure 3.1 Summary of the algorithm of included patients and their mode of diagnosis. For example, patients **A** and **B** who had gastroscopy codes and OG cancer codes within 3 months period where included, whereas patinets **C** and **D** were not included. These excluded cases are likely to be prevalent cases (who were admitted within the current year of study). There might also be a small number of genuine 'incident' cases who were excluded because the episode containing the key primary diagnostic test (index gastroscopy) is 'missing' from their pathway – a coding issue or they went through an atypical diagnostic pathway, perhaps barium radiology or CT scan rather than gastroscopy - this would be uncommon. We considered patient **A** as diagnosed electively although his/her cancer code first appears following emergency admission.

3.3.1 Validation of linkage methods and data outputs:

3.3.1.1 Local validation:

Local validation was important to test the robustness of the OG cancer data extracted from HES, particularly for determining **emergency admission** at the time of diagnosis in which a sample of 143 locally-diagnosed cases of OG cancer was matched with the corresponding data from HES by linking to patients' age (+/- 12 months), gender, general practice code and diagnostic gastroscopy date. This analysis is based on collaboration with the digestive disease unit at Aintree University Hospital [Shawihdi, Stern, et al. 2011]. [294] Locally diagnosed cases were identified from hospital histopathology database, excluding tertiary referrals. 2-year audit periods were defined matching the period of available national data, 2006-08. Local emergency cases were defined as those who had diagnostic endoscopy that was triggered by unplanned attendance/admission to the accident and emergency department (emergency room). This includes patients who were admitted and underwent gastroscopy during an acute hospitalisation and also those who had an outpatient gastroscopy arranged after an unplanned (emergency) presentation to hospital.

3.3.1.2 National validation:

In order to test the reliability of our database inclusions, coding algorithms and linkage methods, we assessed the face-validity of the national cancer patient population extracted from HES data by comparing their characteristics and outcomes with independent reports from the national OG cancer audit [112, 113, 177], cancer research UK [4, 6] and the NCIN[295]. These sources represent the most accurate national data available.

3.4 Results

3.4.1 The extracted episodes of care coded with OG cancer patients and the selection of primary study population.

Of approximately 12 million medical and surgical hospital episodes coded by the national routine data annually, fewer than 8% were excluded owing to invalid data entries (e.g. default/nonsense dates or missing key data fields **(Table 3.1)**. This could indirectly indicate that the process of data "autocleaning" and "validation cycles" created by HES has achieved up to 92.8% accuracy.

Within the study period there were 130,466 episodes had at least one OG cancer related codes (C15, C16). Of these, 33,115 patients were identified – 86.5% using the first diagnostic position alone and 13.5% with the additional analysis of diagnosis positions 2 to 14. As a result of internal linkages within HES though the patients' HESID, 42,397 (32.5%) more episode-related patient information records were obtained which had not been coded for OG cancer **(Table 3.2, Figure 3.2)**.

Table 3.1 Shows the effects of these main data cleaning stages

Clean-up of original HES dataset episodes	**2006/07**	**2007/08**
Dataset containing medical and surgical episodes	**11,580,198**	**12,181,932**
minus blank ages	5699	10296
minus invalid ages	28267	30141
minus under 16's	404875	422100
minus excluded trusts	380273	560307
minus excluded admission methods	3393	3155
Remaining number of episodes	**10,757,691 (92.8%)**	**11,155,933 (91.5%)**

This study provides a well-matched number of episodes coded for OG cancer, as well as the number of individual patients coded at the primary, secondary, or any

other diagnosis position across the two years **(Table 3.2)**. This would suggest that there is no major discrepancy in the coding process between these two data years, and also that the correct application of techniques was used to extract this information.

Table 3.2 Shows the breakdown of numbers from all medical and surgical episodes to the number of individual OG cancer patients (At every diagnosis position).

	2006/07	**2007/08**	**2006/08**
Total medical and surgical episodes	**10,757,691**	**11,155,933**	NA
Episodes with OG cancer codes	**65,027**	**65,439**	**130,466**
Coded at primary position	52,193(80.3%)	50,783(77.6%)	102,975(78.9%)
Coded at secondary position	7,544(11.6%)	8,234(12.6%)	15,778(12.1%)
Coded at any other position (DIAG_3 to DIAG_14)	5,290 (8.1%)	6,422 (9.8%)	11,713 (8.9%)
Individual patients with OG cancer	**18,693**	**19,261**	**33,115**
Coded at primary position	15,829(84.7%)	16,075(83.5%)	28,652(86.5%)
Coded at secondary position	1,752(9.4%)	1,790(9.3%)	2,662(8.0%)
Coded at any other position (DIAG_3 to DIAG_14)	1,112(5.8%)	1,396(7.2%)	1,801(5.4%)
Episodes related to OG cancer patients but without OG cancer related codes	**20,234**	**22,163**	**42,397**

It proved possible to make better use of HES data by identifying all relevant hospital episodes *before* the first appearance of a cancer code in the patients' history. According to the method used **(Figure 3.2)**, the number of patients with coded gastroscopy procedures was 24,659, of which 23521 (95.3%) had their procedure within three months before the initial cancer coding episode of care. Within this patients' cohort we found that 17% (around 1 in 5 cases) were initially coded (at the time of index gastroscopy) with non OG cancer codes. Although some cases coded at a lower order position will be prevalent (established) cases, the rules for the chronological sequence of episodes would exclude them since prevalent cases

would lack the required coding pathway (i.e. with first diagnostic gastroscopy recorded within three months of cancer coding).

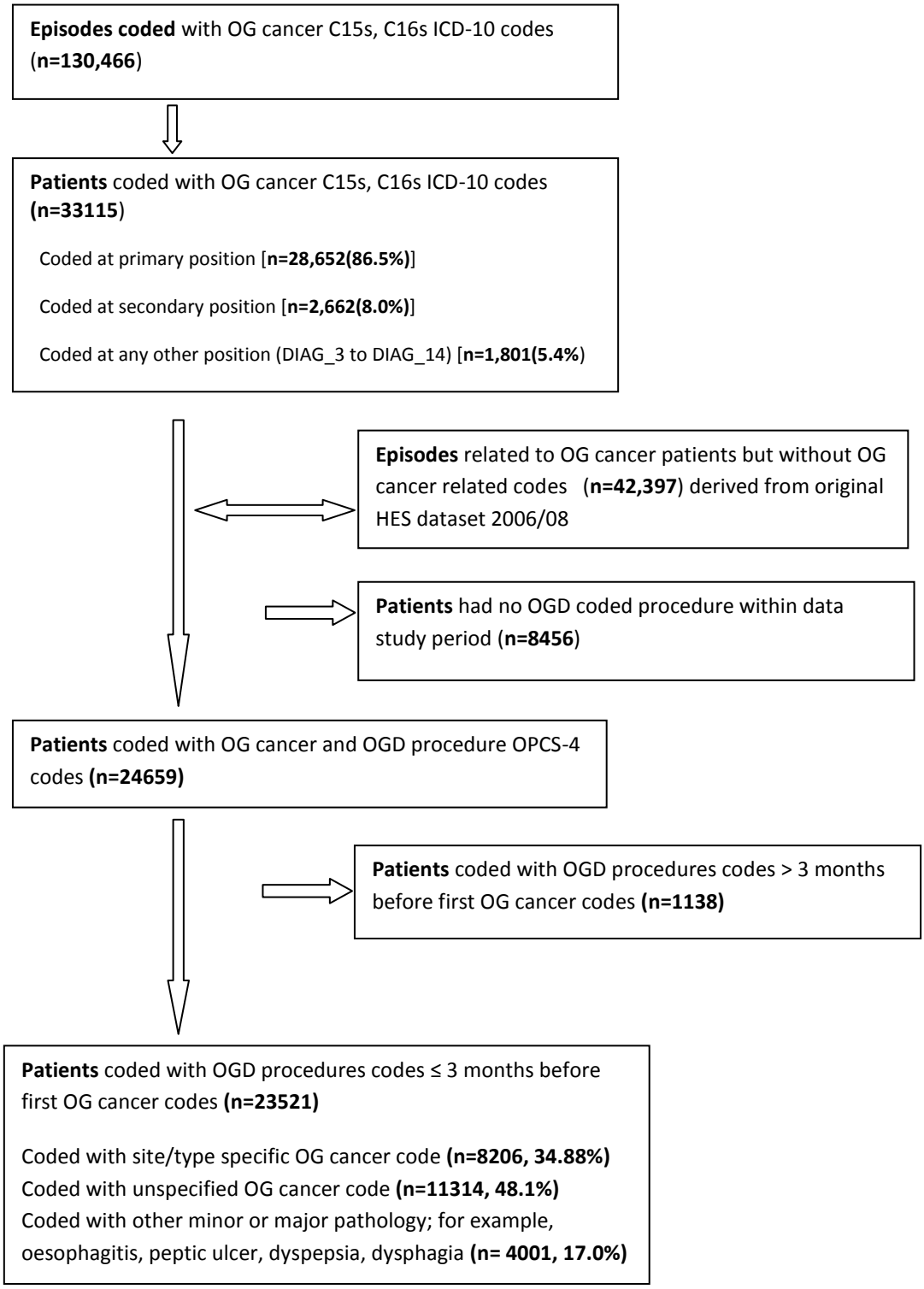


Figure 3.2 OG cancer patients identification process**.**

3.4.2 Number of deaths for patients coded with oesophageal and gastric cancers HES (2006-8)

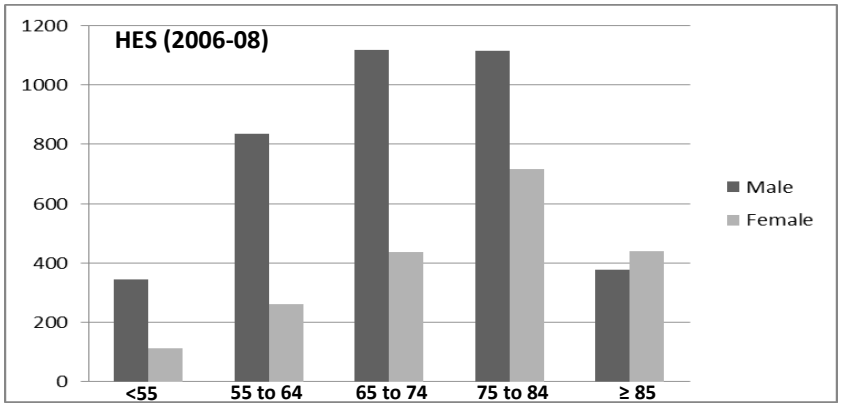
Owing to the external linkages of patients' ONS death dates, **(Tables 3.3, Figures 3.3, 3.4)** show the distribution of the identified number of deaths for any patient coded in HES with oesophageal and gastric cancers, by age groups and gender with the comparison with other published data.

Table 3.3 Shows the number of deaths for patients coded with oesophageal and gastric cancers, by age groups and gender, HES 2006-08

	Oesophageal			Gastric		
	Male	**Female**	**Persons**	**Male**	**Female**	**Persons**
HES (2006-08)[1]	3787	1966	5753	2926	1628	4554

This text box is where the unabridged thesis included the following third party copyrighted material:

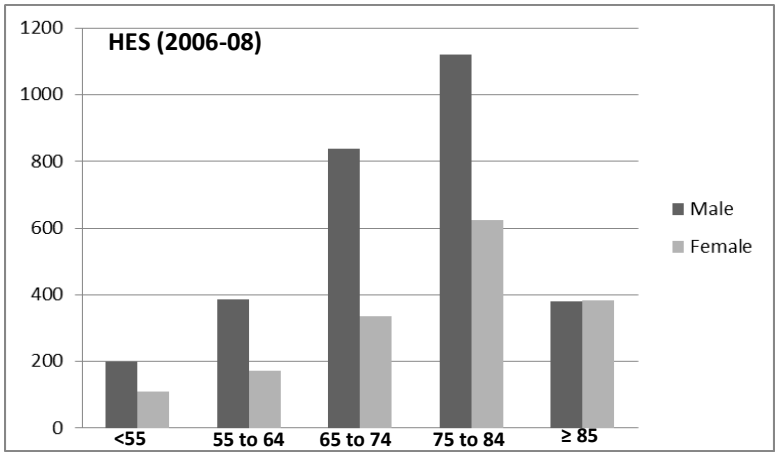
ONS. *Office for National Statistics. Statistical Bulletin. Cancer and mortality in the United Kingdom 2005-2007.* 2010 06/09/2013]. Cancer research UK. Stomach cancer mortality statistics. 24 June 2010 [cited 2013 06/09/2013]; Available from: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/stomach/mortality/. Cancer research UK. Oesophageal cancer mortality statistics 29 April 2010 [cited 2013 06/09/2013]; Available from: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/oesophagus/mortality/.



This text box is where the unabridged thesis included the following third party copyrighted material:

Cancer research UK. Oesophageal cancer mortality statistics 29 April 2010 [cited 2013 06/09/2013]; Available from: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/oesophagus/mortality/.

Figure 3.3 Trends of deaths by gender and age groups for Oesophageal cancer. [297]



This text box is where the unabridged thesis included the following third party copyrighted material:

Cancer research UK. Stomach cancer mortality statistics. 24 June 2010 [cited 2013 06/09/2013]; Available from: http://www.cancerresearchuk.org/cancer-info/cancerstats/types/stomach/mortality/.

Figure 3.4 Trends of deaths by gender and age groups for Gastric cancer.[296]

Furthermore, the number of deaths related to oesophageal and gastric cancers, by age and gender groups have shown similar trends to the UK records published by Cancer Research UK.[296, 297] This suggests a successful external linkages with the ONS death registry data.

3.4.3 Demographic characteristics of cancer cases with a complete care pathway

The counts and demographic characteristics of these cancer cases (n=23521) with a comprehensive clinical care pathway across the two years are summarized in **(Table 3.4).**

Table 3.4 Demographic characteristics of OG cancer patients with a valid pathway of care

	Oesophageal		**Gastric**		**OG cancer**	
Patients n,%	15388	65.4%	8133	34.6%	23521	100%
Age [Mean (SD), median]	71 (12) 72		73 (11) 75		72 (12) 73	
Age groups						
< 55	1394	9.1%	566	7.0%	1960	8.3%
55 to 64	3169	20.6%	1059	13.0%	4228	18.0%
65 to 74	4371	28.4%	2249	27.7%	6620	28.1%
75 to 84	4671	30.4%	3043	37.4%	7714	32.8%
≥ 85	1783	11.6%	1216	15.0%	2999	12.8%
Gender						
Male	10169	66.1%	5323	65.4%	15492	65.9%
Female	5219	33.9%	2810	34.6%	8029	34.1%
Co-morbidity						
No co-morbidity	11761	76.4%	5517	67.8%	17278	73.5%
1 co-morbidity	2542	16.5%	1607	19.8%	4149	17.6%
≥ 2 co-morbidity	1085	7.1%	1009	12.4%	2094	8.9%
Deprivation quintile						
Missing	170	1.1%	74	.9%	244	1.0
1 (Most deprived)	3071	20.0%	1919	23.6%	4990	21.2
2	3130	20.3%	1735	21.3%	4865	20.7
3	3173	20.6%	1635	20.1%	4808	20.4
4	3085	20.0%	1543	19.0%	4628	19.7
5 (Least deprived)	2759	17.9%	1227	15.1%	3986	16.9

3.4.4 Route of diagnosis and outcome of OG Cancer cases in England and the association between patient level factors and outcomes.

Overall, a quarter of cases were diagnosed following emergency hospitalization **(Figure 3.5)**. It can also be seen from the data that a higher percentage of gastric cancers were diagnosed following unplanned emergency admissions.

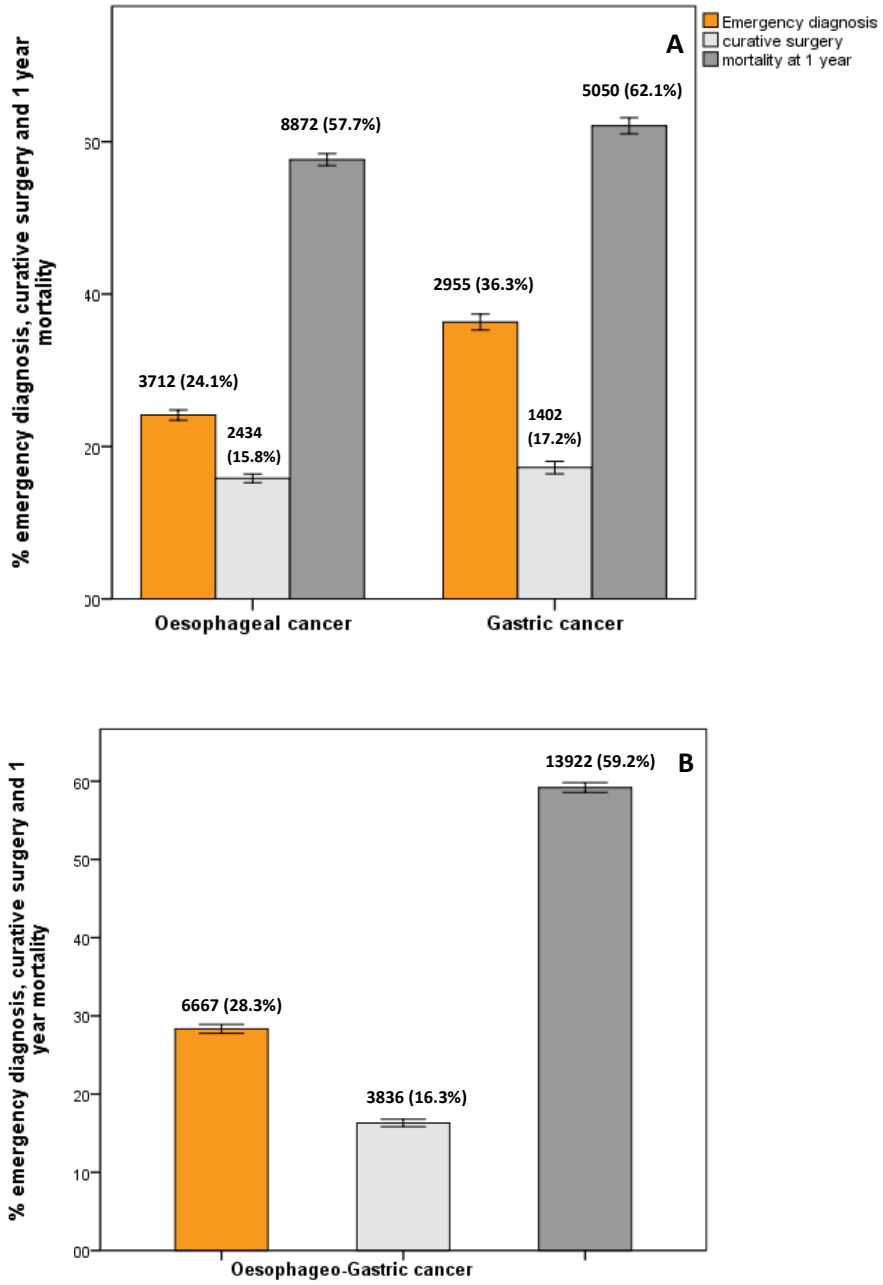


Figure 3.5 The number, percentage and 95% confidence interval of patients diagnosed during emergency admission, patients who had potentially curative surgical resection and patients who died within one year of diagnosis; results are shown for (A) Oesophageal, gastric and (B) Oesophageo-gastric cancer patients' categories.

Further examination of the differences in these outcomes according to age, gender, co-morbidity and those in different deprivation quintiles are explored in **(Tables 3.5, 3.6 and Figure 3.6, 3.7, 3.8)**.

This analysis reveals that the proportions of patients with these outcomes are relatively similar for males and females within each age band. However, females particularly in the older age groups experienced poorer results **(Table 3.5)**. Poorer survival has also been highlighted for those patients diagnosed through the emergency presentation route, for patients who had no major surgical resection and for patients aged 85 and over **(Figure 3.6)**.

Even though most (73.5%) OG cancer patients appeared to have no coded comorbidity either during their index gastroscopy or within their first cancer-coded admission, the remaining (26.5%) patients with comorbidity tended (as expected) to have a worse outcome **(Figure 3.7).**

This data further discloses that with respect to age groups, similar patient trends are distributed across the deprivation quintile **(Figure 3.8)**. However, a higher percentage of the most deprived group of patients was diagnosed during emergencies **(Table 3.6)**.

The highest variation in the deprivation quintile across these outcomes was also among the emergency rote of diagnoses, which showed more than fivefold difference **(Figure 3.9)**. This magnitude of variation might suggest that there could be some degree of inequality in the way these patients are managed, rather than simply differences in the burden of disease. Perhaps this might be due to less

effective use of elective diagnostic services (e.g., gastroscopy) despite its widespread availability.

Table 3.5 The number, percentage of OG cancer patients diagnosed during emergency admission; patients who had potentially curative surgical resection and patients who died within one year of diagnosis. These crude outcomes are shown according to their age groups and gender distribution.

Males	**N**	**Emergency**		**Surgery**		**Mortality 1 year**	
All ages	15,492	4,192	27.0%	2,676	17.2%	9,018	58.2%
< 55	1375	309	22.47%	349	25.38%	655	47.63%
55 to 64	3114	603	19.36%	720	23.12%	1509	48.45%
65 to 74	4728	1093	23.12%	1027	21.72%	2525	53.40%
75 to 84	4822	1542	31.98%	547	11.34%	3227	66.92%
≥ 85	1453	645	44.39%	33	2.27%	1102	75.84%

Females	**N**	**Emergency**		**Surgery**		**Mortality 1 year**	
All ages	8,029	2,475	30.8%	1,160	14.4%	4,904	61.0%
< 55	585	145	24.79%	161	27.52%	264	45.12%
55 to 64	1114	201	18.04%	304	27.29%	541	48.56%
65 to 74	1892	415	21.93%	391	20.67%	999	52.80%
75 to 84	2892	967	33.44%	279	9.65%	1880	65.00%
≥ 85	1546	747	48.32%	25	1.62%	1220	78.91%

Persons	**N**	**Emergency**		**Surgery**		**Mortality 1 year**	
All ages	23,521	6,667	28.30%	3,836	16.30%	13,922	59.20%
< 55	1960	454	23.16%	510	26.02%	919	46.88%
55 to 64	4228	804	19.02%	1024	24.22%	2050	48.48%
65 to 74	6620	1508	22.78%	1418	21.42%	3524	53.23%
75 to 84	7714	2509	32.53%	826	10.71%	5107	66.20%
≥ 85	2999	1392	46.42%	58	1.93%	2322	77.42%

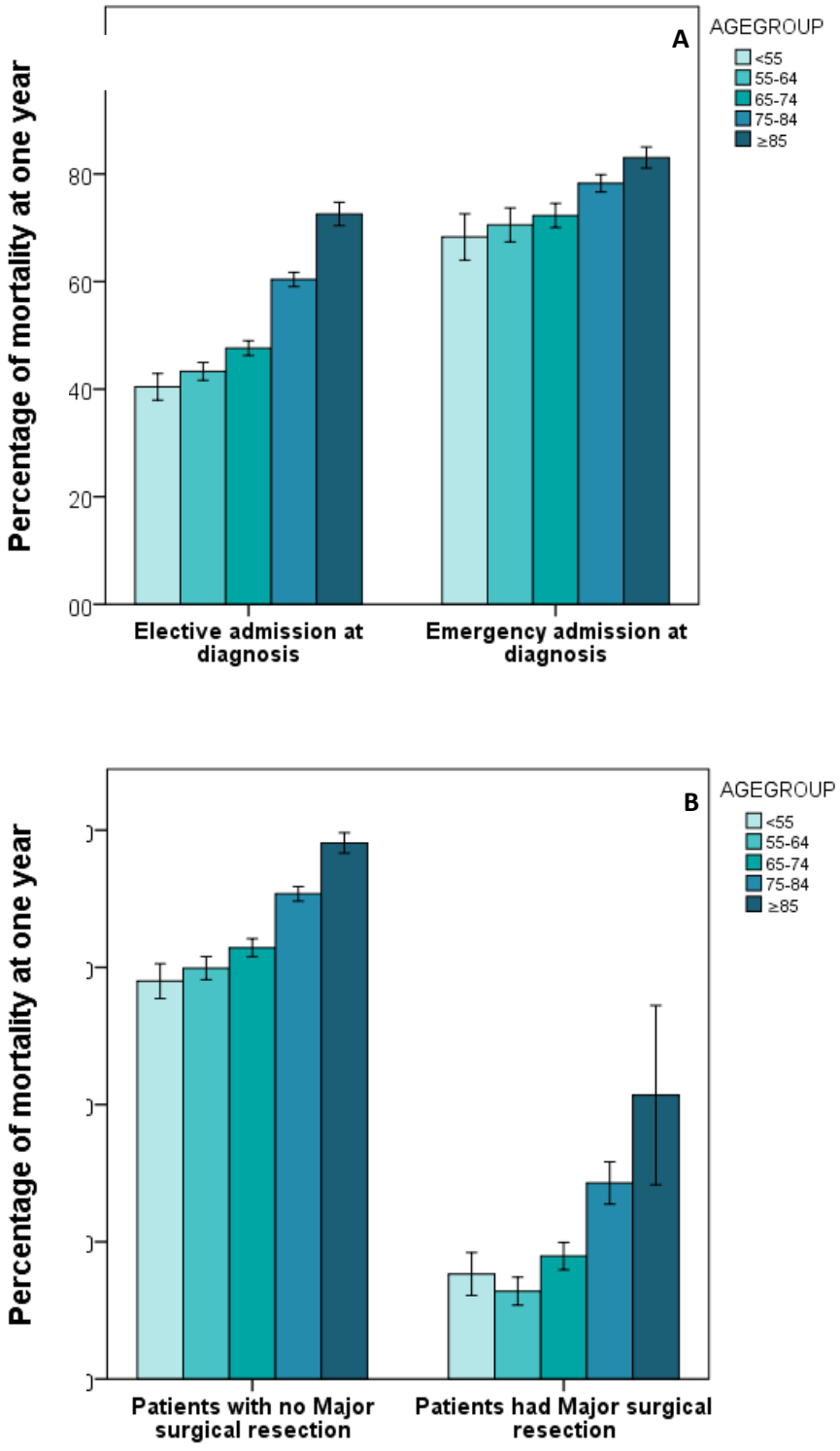
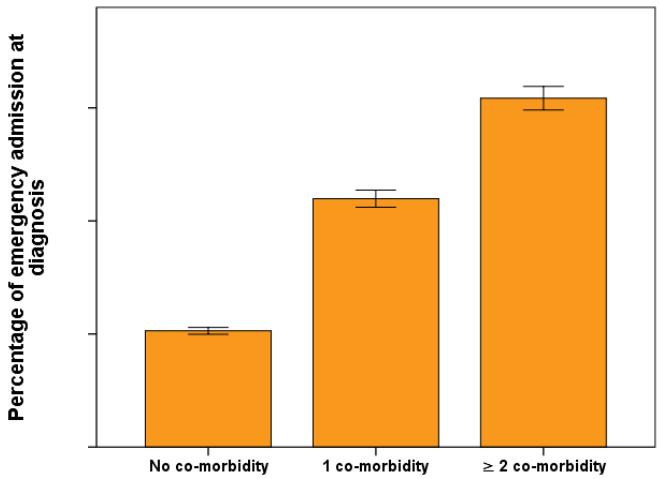
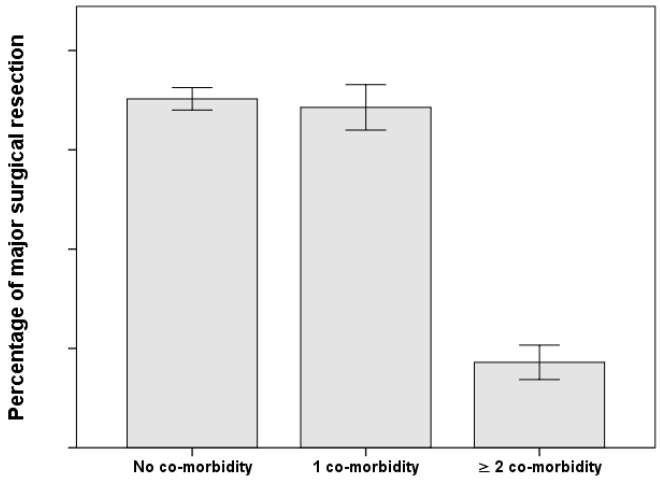


Figure 3.6 Highlights the poorer survival for those patients **(A)** diagnosed through the emergency presentation route, those patients **(B)** who had no major surgical resection and for both **(A)** and **(B)** patients' aged 85 and over.





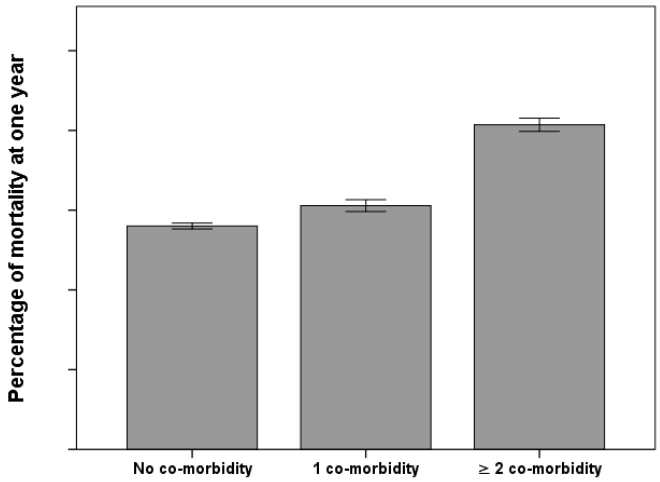


Figure 3.7 Shows the percentages, 95% confidence interval and trends of OG cancer patients' outcomes in relation to patients' co-morbidity groups.

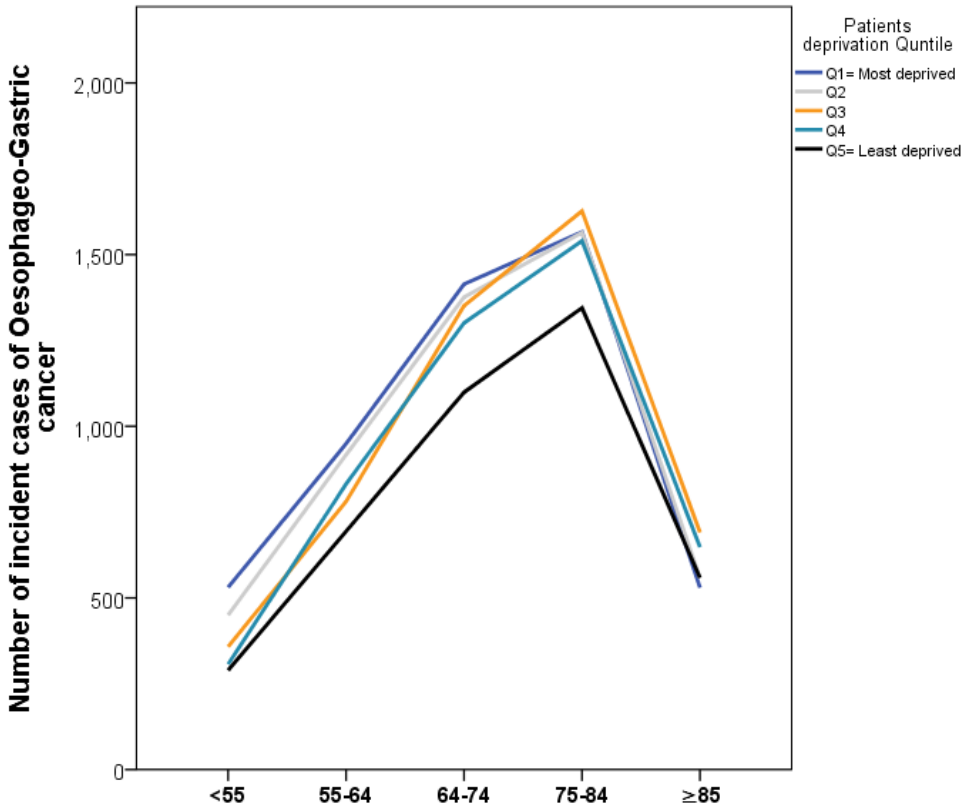


Figure 3.8 The distribution of patients with coded diagnosis compatible with incident cases of OG cancer according to their age groups and by their socioeconomic status.

Table 3.6 OG cancer patients' outcomes in relation to quintiles of patients' level deprivation, as measured by the English Indices of Deprivation 2007

Deprivation quintile	Emergency		Surgery		Mortality 1 year	
Missing	64	1.0%	25	0.7%	95	0.7%
1 (Most deprived)	1625	24.4%	755	19.7%	3055	21.9%
2	1412	21.2%	801	20.9%	2864	20.6%
3	1348	20.2%	778	20.3%	2876	20.7%
4	1211	18.2%	804	21.0%	2704	19.4%
5 (Least deprived)	1007	15.1%	673	17.5%	2328	16.7%

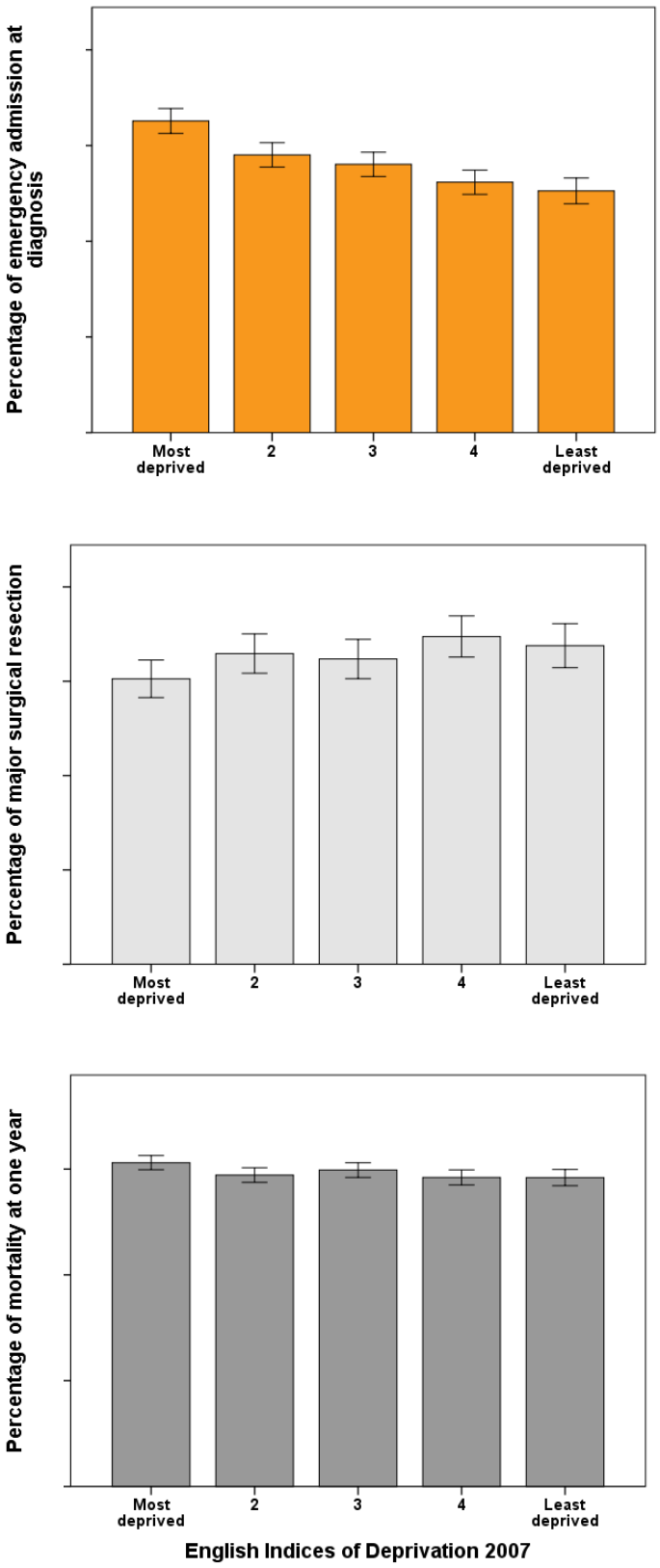
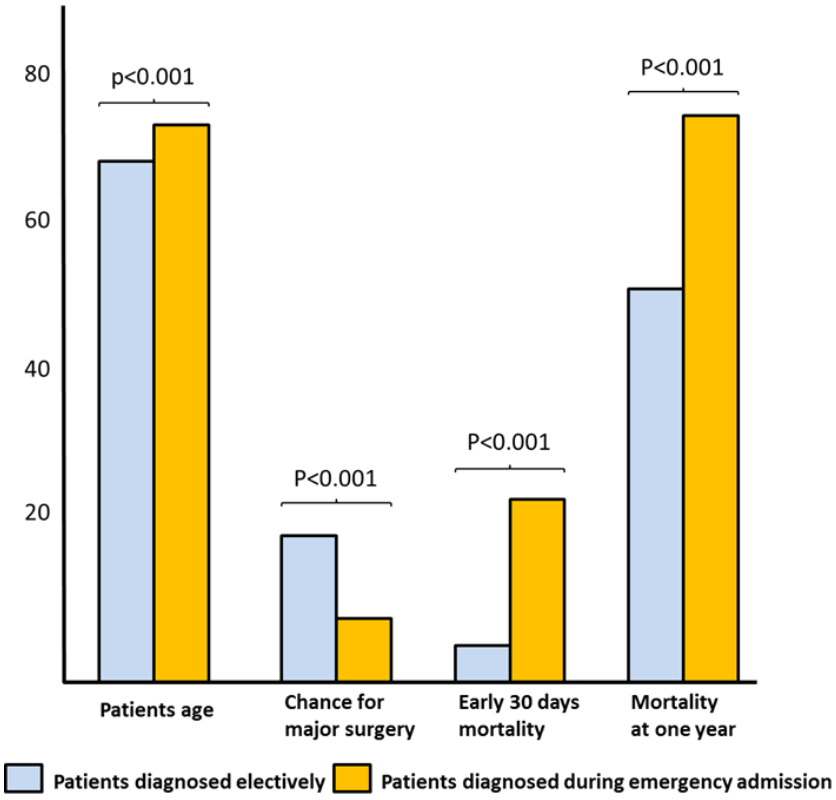


Figure 3.9 Shows the percentages, 95% confidence interval and trends of OG cancer patients diagnosed during emergency admission, patients who had potentially curative surgical resection and patients who died within one year of diagnosis in relation to quintiles of patients' level deprivation as measured by the English Indices of Deprivation 2007.

Emergency patients, as expected were significantly older, with more co-morbidity. These cases also demonstrate a lower chance for potentially curative surgical treatment, higher early mortality and indeed a poorer survival rate at one year **(Figure 3.10)**.



	Diagnosed electively		Diagnosed during emergency admission	
Patients n,%	16,854	71.65%	6,667	28.35%
Age (Mean, SD)	70	11	75	12
Gender				
Male	11300	67.0%	4192	62.9%
Female	5554	33.0%	2475	37.1%
Co-morbidity groups				
No co-morbidity	13726	81.4%	3552	53.3%
1 co-morbidity	2326	13.8%	1823	27.3%
≥ 2 co-morbidity	802	4.8%	1292	19.4%
Chance for major surgery	3294	19.5%	542	8.1%
Early 30 days mortality	723	4.3%	1626	24.4%
Survival at 1 year	8019	47.6%	1580	23.7%

Figure 3.10 Route of diagnosis (elective Vs. emergency) and outcomes for OG cancer patients

The Kaplan-Maier survival curves for these patients confirm an early and persistent separation between different routes **(Figure 3.11**, Log Rank p<0.001**)**. Whilst the survival curves separate when the data is split into the different modes of admission, the differences remain significant, regardless of tumour site. Survival curves for oesophageal and gastric cancer are shown. **(Figure 3.12**)

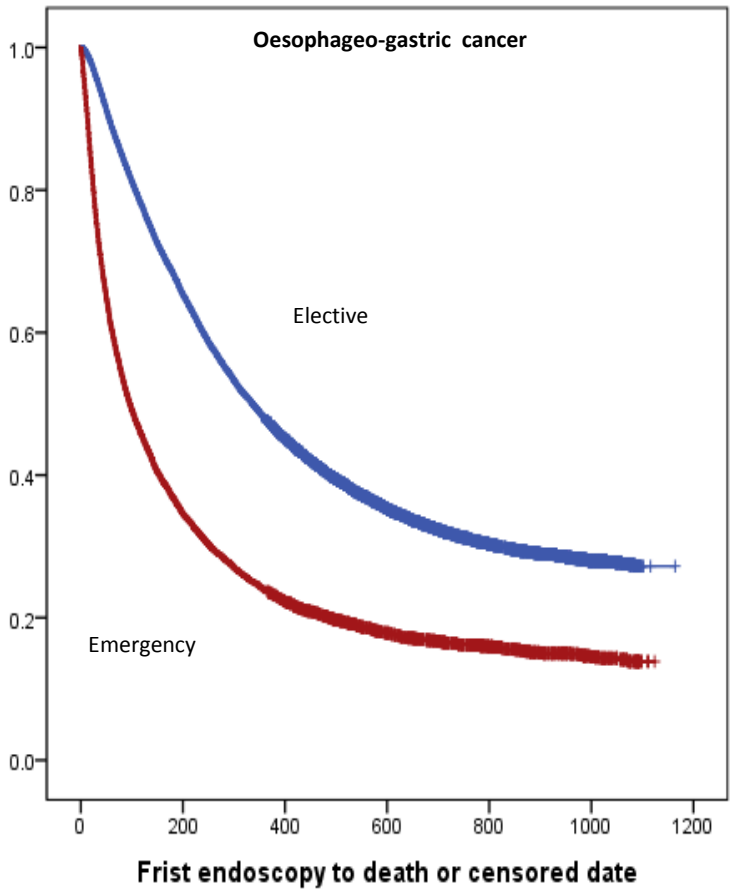
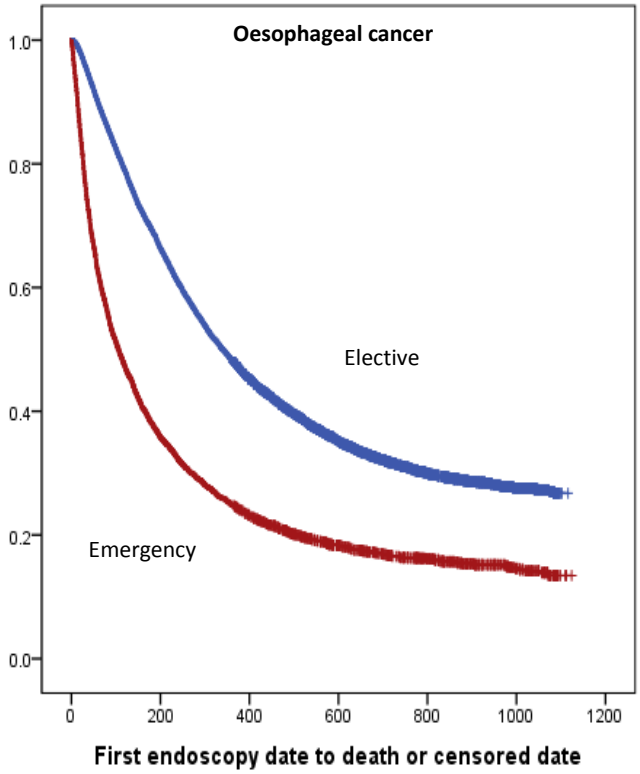


Figure 3.11 Kaplan-Maier survival curves for OG cancer patients according to their mode of diagnostic admission (emergency vs. elective)



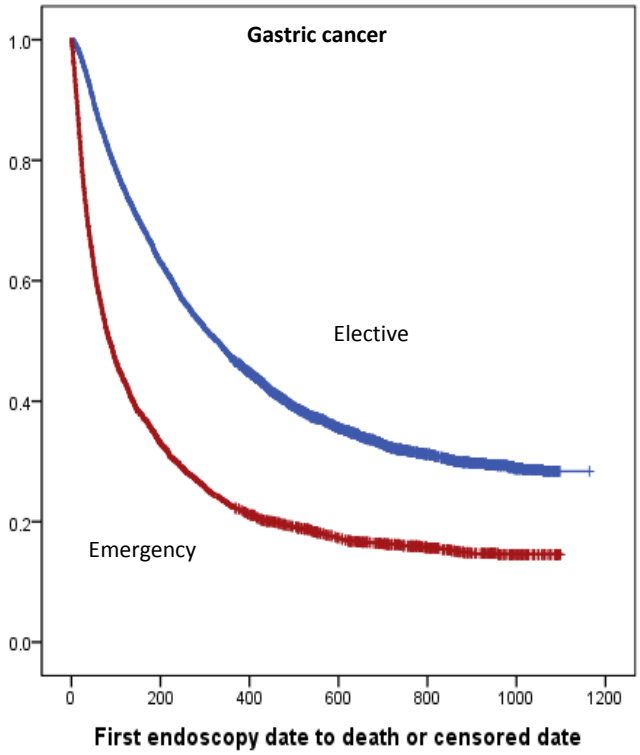


Figure 3.12 Kaplan-Maier survival curves for oesophageal and gastric cancer patients according to their mode of diagnostic admission (emergency vs. elective)

3.4.5 Validation of the OG cancer patient population extracted from HES

The linkage methodology used in our 2-year data period identified 23,521 cancer cases. This equates to 11,761 new cases in England per year. This compares favourably (90.7%) to an annual figure of 12,957 reported by the NCIN for the whole of England [295] and (91.3%) with the ONS published annual figure of 12873. [15] Such differences could be explained by the fact that for some patients the key primary diagnostic test (index gastroscopy) is 'missing' from their HES coded pathway. It is highly unlikely that such differences could bias the overall results because, first they are in small number (less that 9%) and secondly these excluded cases shared similar demographic characteristics to that of the included ones (i.e. no significant difference in age or gender profile). No systematic bias in favour of the main hypothesis would be expected from studying a representative sample of over 90% of national cases. By contrast, case ascertainment in the National Oesophagogastric Cancer Audit was under 70%.[113]

Patients' sex distribution, median age, and the percentage of patients under the age of 55 in this cohort were consistent with the same figures reported for cases in the National Oesophago-gastric Cancer Audit [112, 113, 177, 298]. Numerous studies in various populations have also shown an association between socioeconomic deprivation status and risk of OG cancer [65] in keeping with our results.

Similarly, this study defined the mode of admission by identifying the first clinically *relevant* episode of care in the patient pathway. Consequently, the percentage of OG cancer patients who were first admitted through the emergency route is 28.3%

(24.4% of oesophageal and 36.1% of gastric). Such proportions are very comparable with the information published by the NCIN, which reports that around a quarter (26%) of OG cancer patients (21% of oesophageal and 32% of gastric cancers) were diagnosed during emergency admissions within the same time period [275, 299].

With respect to the other outcome variables, the resultant national rate of major surgical resection is 16.5% for OG cancers overall (15.5% reported by NCIN) [277], and the one-year survival rate following index gastroscopy is 40.7% (41.14% reported by the NCIN). [295] The close agreement of our data outputs with independent analyses of national cancer data, suggesting valid methodology.

The linkage methodology has further been verified by the use of a local audit dataset, indicating that within the matched patient population between our local hospital and HES, the accuracy of method of admission, coded surgical resection date as well as death date were consistent in 141 (98.6%), 137 (93.8%) and 140 (97.9%) cases respectively.

3.4.6 Patients factors associated with OG cancer outcome in England

Binary Logistic Regression confirms that patients' age, co-morbidity and deprivation are independent predictors of cancer diagnoses through the emergency presentation route, with potential chance for major surgical resection and mortality at 12 months in our national cohort, with gender not being a significant factor **(Table 3.7, Figures 3.13, 3.14, and 3.15)**.

Table 3.7 Patients factors associated with OG cancer outcome in England (n=23,521). adjusted odds ratios with 95% CI based on **Uni-variate** logistic regression (Reference group = 1)

Variable	Emergency Admission			Major Surgical Resection			Death within 12 months		
	OR	CI	p	OR	CI	p	OR	CI	p
Age									
< 55	**1**	-	-	**1**	-	-	**1**	-	-
55 to 64	0.77	0.68-0.88	<0.001	0.90	0.80-1.02	0.127	1.06	0.95-1.18	0.242
65 to 74	0.97	0.86-1.10	.722	0.77	0.69-0.87	<0.001	1.28	1.16-1.42	<0.001
75 to 84	1.59	1.42-1.79	<0.001	0.34	0.30-0.38	<0.001	2.21	2.00-2.45	<0.001
≥ 85	2.87	2.53-3.26	<0.001	0.05	0.04-0.07	<0.001	3.88	3.43-4.39	<0.001
Gender									
Female	**1**	-	-	**1**	-	-	**1**	-	-
Male	0.83	0.78-0.88	<0.001	0.80	0.75-0.87	<0.001	0.88	0.84-0.93	<0.001
Co-morbidity									
No co-morbidity	**1**	-	-	**1**	-	-	**1**	-	-
1 co-morbidity	3.02	2.81-3.25	<0.001	0.97	0.88-1.06	.514	1.23	1.15-1.32	<0.001
≥ 2 co-morbidity	6.22	5.65-6.84	<0.001	0.21	0.17-0.26	<0.001	3.44	3.06-3.85	<0.001
GP Practices Deprivation									
1 Most deprived	**1**	-	-	**1**	-	-	**1**	-	-
2	0.84	0.77-0.92	<0.001	1.10	0.99-1.23	.069	0.90	0.83-0.98	0.017
3	0.80	0.74-0.88	<0.001	1.08	0.97-1.20	.152	0.94	0.86-1.02	0.155
4	0.73	0.67-0.80	<0.001	1.17	1.05-1.31	0.003	0.89	0.82-0.96	0.005
5 Least deprived	0.70	0.63-0.76	<0.001	1.13	1.01-1.27	0.024	0.88	0.81-0.96	0.007

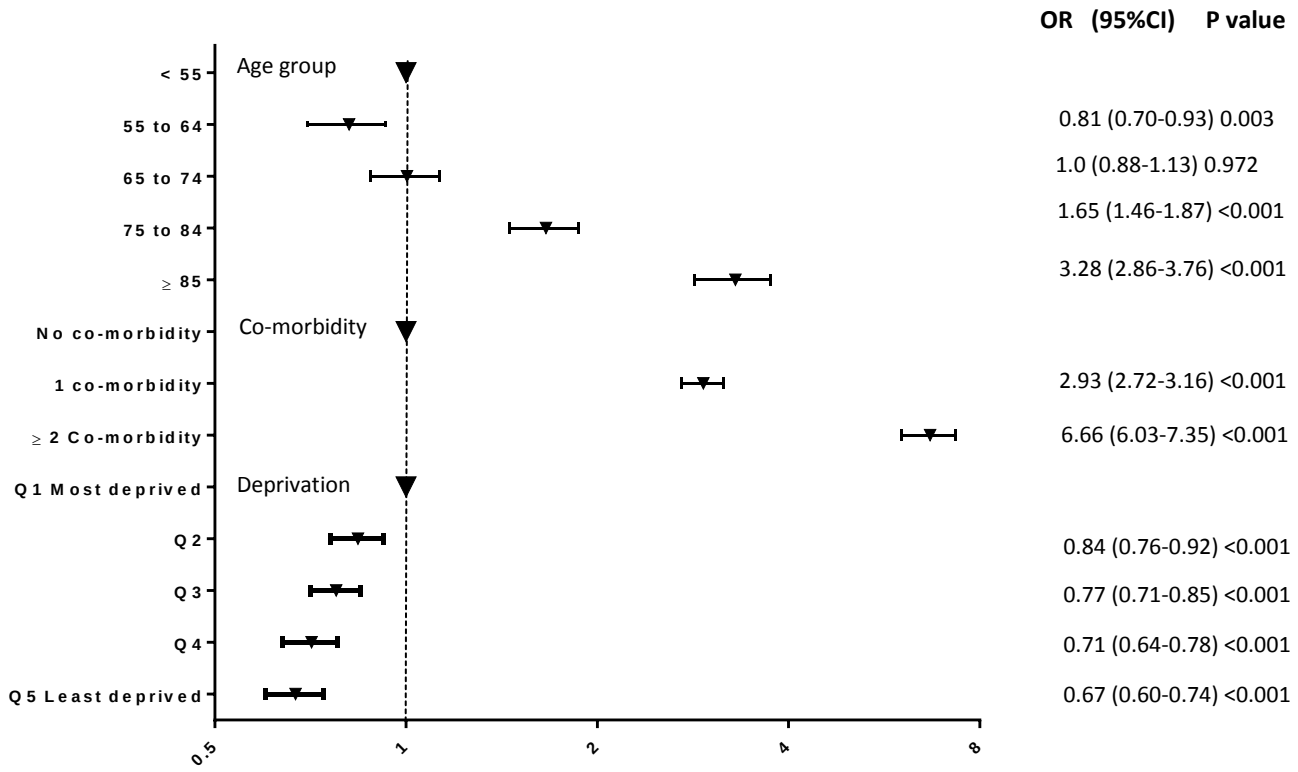


Figure 3.13 Patients factors (Age, Gender, Comorbidity and Deprivation) associated with emergency route of diagnosis for (n=23,521) cases of OG cancer in England. Odds ratios with 95% CI based on **multivariate** logistic regression (Reference group = ▼). Gender was not a predictor for patient's outcome; hence it is omitted from the regression equation.

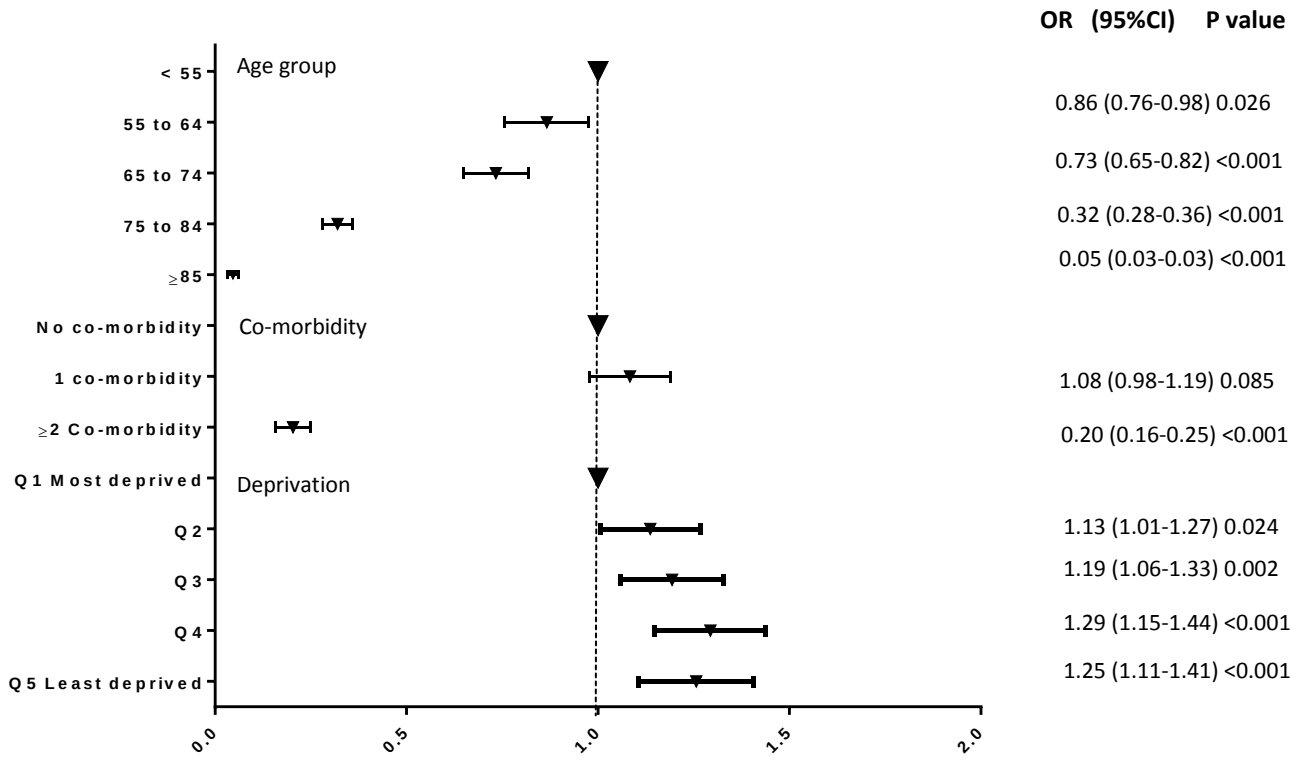


Figure 3.14 Patients factors (Age, Gender, Comorbidity and Deprivation) associated with major surgical resection for (n=23,521) cases of OG cancer in England. Odds ratios with 95% CI based on **multivariate** logistic regression (Reference group = ▼). Gender was not a predictor for patient's outcome; hence it is omitted from the regression equation.

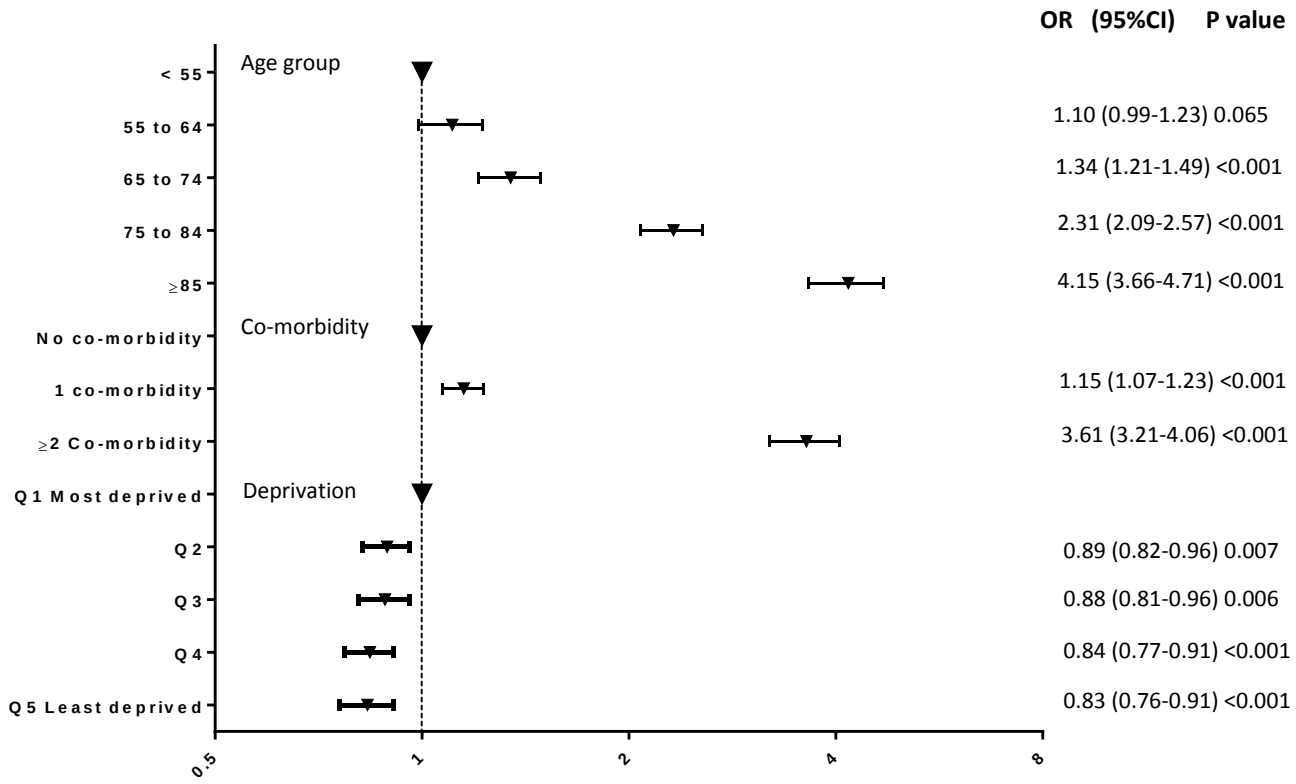


Figure 3.15 Patients factors (Age, Gender, Comorbidity and Deprivation) associated with death at 12 month for (n=23,521) cases of OG cancer in England. Odds ratios with 95% CI based on **multivariate** logistic regression (Reference group = ▼). Gender was not a predictor for patient's outcome; hence it is omitted from the regression equation.

3.5 Discussion:

This chapter illustrates at national level that the total case numbers, demographic characteristics and measured outcome variables for the 'incident' patient cohort extracted from HES data are consistent with external independent analyses of available data for OG cancer in England. Furthermore, by linking cases at one hospital to an audit database containing information from the local clinical records, it was possible to show close agreement between outcome variables (emergency admission; surgery; mortality) assigned using our algorithms in HES data and the 'real' outcome recorded in the local records. These face-validity checks suggest that careful application of clinical logic to the HES dataset can generate novel methods for overcoming the limitations of HES data such as lack of diagnosis date and the varied manner in which cancer cases may be coded diagnostically during the early phase of their pathway.

The methods development phase of the research tested the possibility of finding a more reliable starting point for the OG cancer patient journey within the sequence of coded episodes contained within HES data. As mentioned in Chapter 1, the main diagnostic investigation for this type of malignancy is gastroscopy with biopsy (OGD) followed by histological processing and reporting to confirm the diagnosis [100, 115, 300, 301]. HES data lacks the histopathology report or formal diagnostic date. This makes the use of the 'first coding date' for cancer (i.e. the admission or discharge date taken from the episode containing the first recording of a cancer code for the patient) an unreliable indicator for the start of the patient journey for some patients. Thus, our novel method for identifying the 'first' relevant episode of

care in the cancer patient pathway was to flag the first coded diagnostic gastroscopy. Although this index gastroscopy episode frequently contained the first appearance of a relevant OG cancer diagnostic code for that case, we found that 17% of OG cancer cases captured by our methodology had other diagnostic codes recorded at first gastroscopy (e.g. gastric ulcer or oesophageal stricture), with the cancer code appearing at a subsequent episode (e.g. a repeat admission for stenting or surgery). This confirms the unreliable nature of relying only on first appearance of cancer code to identify the start of the pathway.

Having successfully generated a valid cancer population, this study sought to explore the association between the measured cancer outcomes and the described patient-level variables such as age, sex, co-morbidity and deprivation status. As expected, analysis of patient characteristics and outcomes according to mode of admission (emergency or elective) confirmed that patients diagnosed during emergency admission were significantly older (75 vs 70), had more co-morbidity and a lower chance for potentially curative surgical treatment (8.1% vs 19.5%), and showed higher early mortality and indeed poorer survival (23.7% vs 47.6%). We were able to compare these national patterns observed in HES data with an audit study of local cancer outcomes, which showed that locally diagnosed emergency cases were again older than elective (76.0 v 70.4 yrs; $p<0.003$), were less likely to have curative treatment (13.6% v 33.3%; $p<0.013$) and their median survival (138 v 237 days, $p=0.07$) was also shorter. [294, 302]

We further performed multiple logistic regression analysis to test whether there are associations between various patient-level factors available in HES (patients' age,

gender, co-morbidity and deprivation) and the three cancer outcomes measured in this study. This confirmed the anticipated trends that poorer cancer outcomes are associated with advancing age, increased co-morbidity and higher levels of patient deprivation.

It was not possible to report accurate data for individual tumour sites (i.e. oesophageal, junctional, distal gastric). In general, we considered it more useful to study the OG cancer sites collectively since oesophageal and gastric cancer share common signs, symptoms, primary modality of diagnostic testing (gastroscopy) and referral guidelines. A high proportion of cases are also coded in HES under the least-specific codes (C159 and C169) and sometimes with a mixed codes for both cancers. This creates difficulties in the analysis of specific tumour sub-location, particularly for the gastro-oesophageal junction. Similar limitations have also been noted by many published studies used both HES and national cancer registry data [22, 112, 303-305]. However, the primary objectives of the research did not require the ability to extract tumour-site specific information.

Another possible limitation relates to the minority of patients managed privately, information for whom is not available in HES [277]. Hence, incident patients who had their diagnostic gastroscopy in the private sector would not be identified.

Although our rates of emergency admission during the diagnostic pathway were very close to those reported by the NCIN, it is noted that the National Oesophago-gastric Cancer Audit reported lower percentages of emergency diagnosis for both cancers than our data. However, this might be due to the recognised low rate of

case ascertainment achieved in the audit, leading to concerns about inclusion/exclusion bias. The national figures nevertheless still show the same trend that emergency diagnosis is somewhat more prevalent for gastric cancer than for oesophageal cancer (accepting the limitations of site-specific analysis in our own data), and emergency patients tend to have a lesser chance for curative treatment (17% v 39%) [113, 302] which is again similar to our own results.

Deprivation is an important potential determinant of healthcare outcomes. The English IMD scores are derived from 38 indicators grouped into seven empirically weighted domains used to rank each LSOA from the least to the most deprived. Grouping of LSOAs into quintiles is the standard approach taken when generating ordinal categorical variables for socioeconomic status based on IMD. [306] The terminology adopted to describe the deprivation quintiles ("most deprived" to "least deprived") is also in widespread use in the HES-related literature. [240, 268]

Although the percentages of these outcomes by deprivation quintile have not been standardized for differences in the age structure within each quintile, our data still shows that higher percentage of the most deprived group of patients were diagnosed during emergencies, had fewer surgeries and a relatively higher mortality at one year compared with the least deprived groups. Equivalent findings have been reported by the NCIN for both cancers using multiple datasets, including HES. [274, 276, 277]

The highest inequality by deprivation quintile within these outcomes was among the emergency diagnoses. Additional analyses are thus required to explain the causes underlying this observation. The recent Routes to Diagnosis, 2006-2008 (NCIN) suggested that this difference is threefold for oesophageal cancer and tenfold for the gastric cancer population. [276]

The main challenge in this study related to the general issue concerning the completeness, precision and depth of routine administrative coding. However, our methodological approach has striven to overcome such limitations by identifying, linking and chronological ordering of all individual patients care episodes to limit the acknowledged potential impact of coding error. [248, 255, 257, 264, 283].

We were unable to study the frequencies and percentages of each specific tumour pathological type as a result of absence of important clinical details in HES data (i.e. pathology reports) and the use of less specific cancer codes. This information would be of descriptive interest given the changing epidemiology of oesophageal tumour types [2, 16, 22, 307, 308] but is not a requisite for studying factors associated with overall OG cancer outcomes.

Other limitations are related to the lack of tumour staging in the main HES data. Although emergency admission during the diagnostic pathway may be unavoidable for a minority of clinical presentations of OG cancer (e.g. acute GI bleeding), it is important to note that this outcome is being taken as a proxy measure for diagnostic delay as well as an indication of advanced disease. Similarly, the rate of major surgical resection is reflective of earlier diagnosis, since only individuals with

early stage OG cancer will be candidates for potentially curative major resection. Hence, this project assumes that emergency admission at diagnosis, as well as the chance for obtaining surgical resection, are surrogate markers of patients' stage at the time of diagnosis.

Concluding statement:

The results presented for this 'methodological development' phase of work do support the idea that HES data can provide a powerful tool for health services and epidemiologic research if analysed carefully using clinical logic. By applying knowledge of the disease process and care pathways and insight into the limitations of the dataset (e.g. the variety of ways that cases might be coded over time), a bespoke method was generated and tested. The national-level analysis has generated 'real-world' descriptive statistics for OG cancer care in England that exhibit close agreement with independent published sources for national case number, demographics and key outcomes. The cohort exhibits the expected associations between cancer outcome and patient-level sociodemographic (age; sex; deprivation) and co-morbidity variables. The resulting master dataset of cancer cases for 2006-2008 provides the platform for exploring factors associated with OG cancer outcomes in England.

The next chapter describes the results of additional work to generate methods for analysing rates of elective gastroscopy at the level of individual general practices and describes this variation. By linking the master dataset for cancer cases and the GP practice-level data for gastroscopy rates, it is then possible to build a series of univariate, stratified and multiple variable binary logistic regression analyses (with

extensive sensitivity analyses) to test the main study question in a national-scale ecological study – 'Is there an association between rates of gastroscopy in general practice populations and OG cancer outcome?'

Chapter 4 Variation in elective gastroscopy rates in English general practices and outcomes for oesophago-gastric cancer: retrospective analysis of Hospital Episode Statistics

4.1 Introduction

Gastroscopy is the gold standard investigation for identifying serious causes of dyspepsia. This test is relatively expensive, uncomfortable and not without small risk. In England, to a great extent, most of the referral for upper GI endoscopy is made through primary care. Direct access to gastroscopy from primary care was established during the 1980s,[136] and fast-track access for those with alarm symptoms was introduced into the NHS more than 10 years ago under the National Cancer Plan. [108, 309] However, there has been little improvement in the detection of curable cancer over this period. Overall, approximately three-quarters of cases of OG cancer are diagnosed at a late and inoperable stage in the UK. [33, 177]

Given the unresolved questions regarding the value of gastroscopy both in managing dyspepsia and in detecting curable cancer, variation in the rates of gastroscopy across primary care is inevitable. The recent NHS Atlas of Variation also demonstrates that such degrees of variation observed for both cancer diagnosis and gastroscopy were greater than can be explained by variations in the incidence and prevalence of disease. [185, 186]

Analysis of gastroscopy activity data for Primary Care Trusts (PCT) shows more than a twofold range across England.[185] However, this study believes that aggregated data for groups of practices may mask wider variation between individual general practice centres. Assessment of access to this gold standard investigation according to patient outcomes, rather than according to the availability or utilisation of this diagnostic service, is lacking. Hence, showing cancer outcomes at the two ends of

the variation spectrum at GP practice level might provide some promising answers that could yet support the role of this procedure in managing patients with suspected OG cancer.

4.2 Aim

This chapter aims to test the hypothesis that outcomes for OG cancer patients may be associated with local rates of gastroscopy in the general practice population. We postulated that general practices with relatively low per capita rates of gastroscopy may be less likely to identify curable cancers, whereas those with higher levels of gastroscopy may increase the chance of earlier diagnosis and curative treatment.

4.3 Objectives

- To identify general practices in England with validated incident OG cancer cases as described in chapter 3
- To explore the variation of gastroscopy rates at the general practice level after adjustment for the practice registered population demographics.
- To test whether gastroscopy rates in general practice populations in England are associated with the outcome for OG cancer patients. These outcome variables include emergency admission during the diagnostic pathway, the chance for major surgical resection and mortality at twelve months. Any association between local rates of gastroscopy and outcome should be independent of possible confounders such as age and deprivation.

4.4 Method

4.4.1 The eligibility criteria for general practices included in the study

Per capita gastroscopy volume was determined by extracting diagnostic gastroscopy procedures from our previously described two year download of HES data **(chapter 2)**. Procedures were then aggregated at GP practice level. Details of the codes and standardization methods for gastroscopy rate used are also described in **(chapter 2)**.

GP practices in England with a known population list size were (n=**8,338**). [278] Matching of the unique GP practice code with that recorded in our two year download of HES data showed that the number of practices with at least one OGD procedure coded in HES was (n=**8,250**) in which (n=**8,232**) of them had at least one **elective** gastroscopy. This group of practices was subsequently linked to practices with OG cancer coded diagnosis, revealing that (n= **7,217**) of them had at least one prevalent coded OG cancer case, of which (n= **6,650**) practices were related to cancer patients with valid care pathways (Incidence cases are described in chapter 3). With regards to the practice deprivation IMD scores [279], around 137 practices were lacking essential information, leaving just (n= **6,513**) eligible practices for the final analysis **(Figure 4.1)**. These practices were ranked nationally according to their age- and sex-adjusted annual gastroscopy rate and then divided into tertiles (low, medium and high tertiles).

In England GP practice size varies from single handed general practitioner to multi-partner practices and may change from one year to another.[310] It has also been reported that over the last decades more GPs are arranged to work in larger practices by the fact that the number of practices decreased by around 9% from 1997 to 2007. For these reasons, the selected practices in this study were further checked for any major alterations in their total adult list size within the corresponding data years (2006/7 to 2007/8). This step was performed using data supplied by the Health and Social Care Information Centre for the two data years which showed close agreement in year-to-year populations for the study practices over this period.

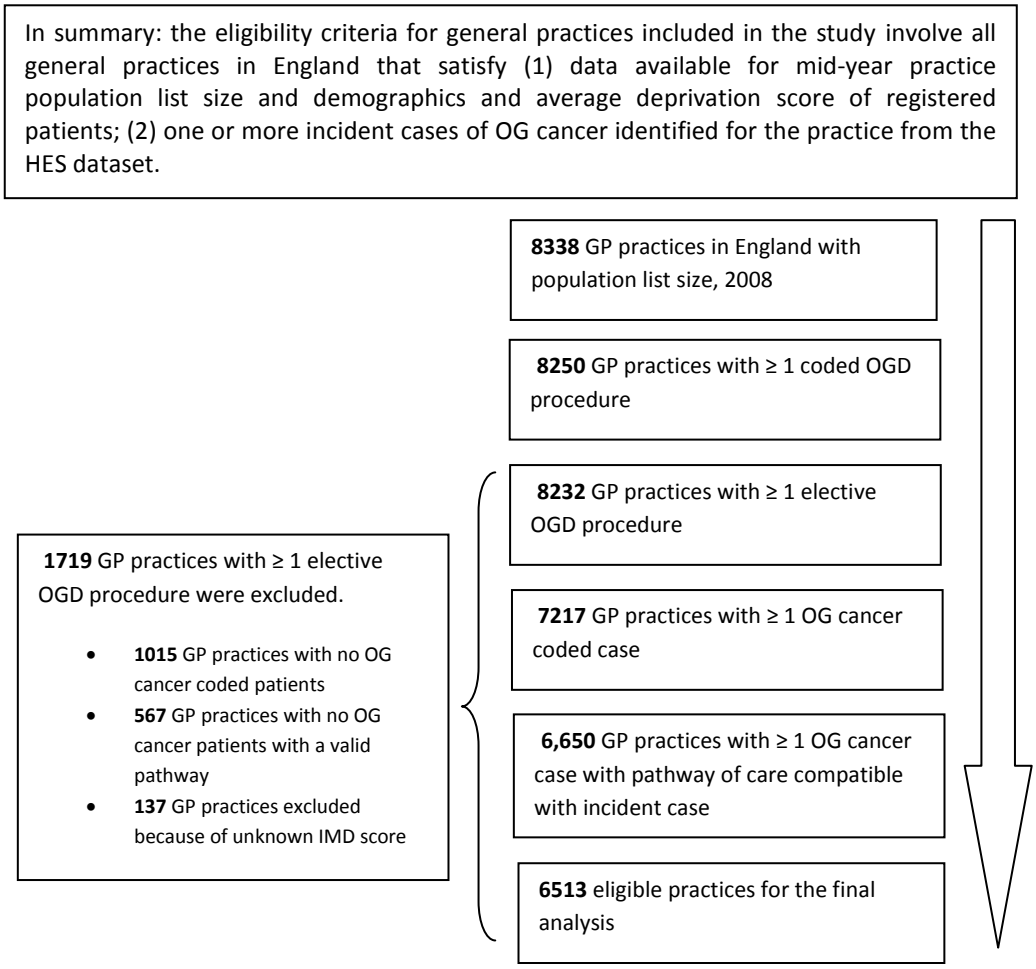


Figure 4.1 The eligibility criteria for general practices included in the study

4.4.2 OG cancer outcome

All general practices in England with incident cases of OG cancer as defined in chapter 3 were combined with their total elective diagnostic gastroscopy activity. Outcome measures for cancer cases were: emergency admission during diagnostic pathway; major surgical resection; and mortality at 1 year. The origin, definition and process of extraction and validation of these outcomes were described in chapters 2 and 3. The origin and methods of extraction of both patients and practice level factors used in this part of study are also described in the section on method **(chapter 2)**. Although the inequality in patients outcome according to the

patients' factors are reported in chapter 3, in the present chapter it is necessary also to use these patients' casemix with other possible practice level covariates in the regression model, to test whether gastroscopy rates at the practice level tertile (exposure of interest) could also act as an independent predictor of patient outcomes **(Figure 4.2.)**.

4.4.3 Statistical analysis:

Unless stated, analysis of variance (ANOVA) and $\chi 2$ tests have been used to compare differences in continuous and categorical variables between the three groups of practices. Univariate logistic regression was used to identify factors associated with patient outcomes. Factors with a significance level of ≤ 0.1 on univariate analysis were included in the final multivariate regression model.

4.4.4 Sensitivity analysis:

Several additional multivariate analyses using an alternative 'exposure' variable to express the gastroscopy rate of the patients' general practice were undertaken. First, this was done by substituting the elective gastroscopy rate tertiles for quintiles and reassigning each practice to one of five groups, according to their rank order of age-sex-adjusted elective gastroscopy per capita. Second, we reassigned each practice to a quintile based on the gastroscopy rate for people over the age of 55 years. This age cut-off reflects the rate of gastroscopy performed in the 'higher risk' population for cancer as identified in recent guidelines. Third, we substituted the practice level categorical variable (tertile or quintile group) for a continuous

scale variable reflecting the actual rate of gastroscopy at the practice (expressed as a rate per 100 to simplify interpretation of ORs).

The NHS Atlas reported the variation in the rate of gastroscopy procedures at the level of primary care trusts (PCT) across all the 152 PCTs in England and then applied an arbitrary exclusion of five (about 3%) PCTs from each end of the referral spectrum.[x] In the present study, no arbitrary exclusion of the highest or lowest 3% of referring practices was applied, since this was judged unnecessary given the grouping of practices into tertiles or quintiles rather than studying individual practices. However, had we excluded 3% of practices from each end of the 6,513 practices included in this study, there would have been no change to the calculated national average rate of gastroscopy nor any change to the magnitude of variation shown across the tertile or quintile groupings.

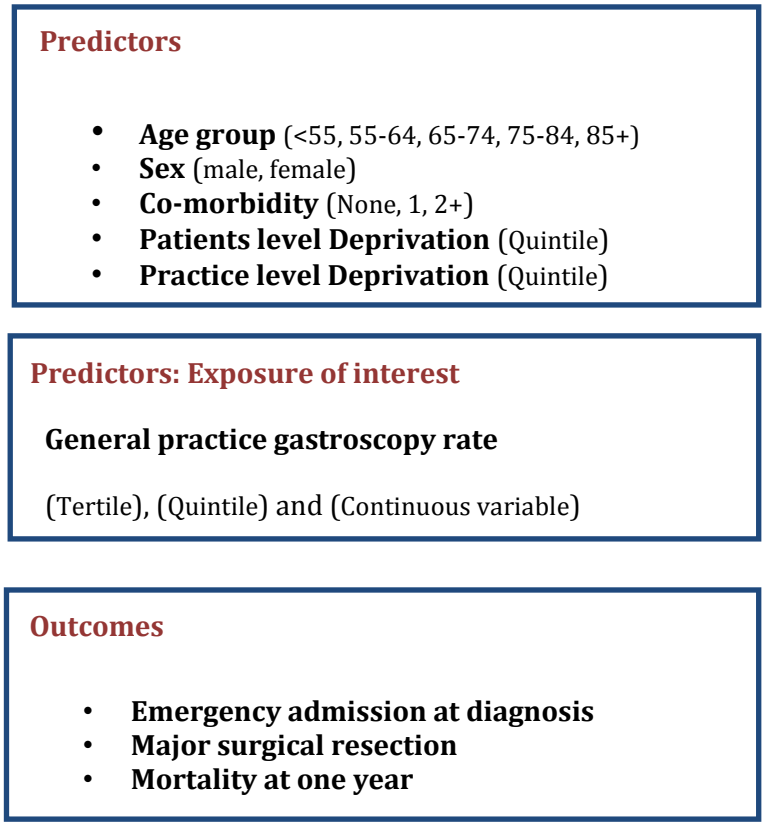


Figure 4.2 Illustrates the regression model to test whether gastroscopy rate at the practice level (exposure of interest) could also act as an independent predictor of patient outcomes after adjusting for the possible covariates.

4.5 Results

4.5.1 General practices included in the study and their rates of elective gastroscopy

During the study period, there were 6,513 general practices eligible for this analysis. These practices served a total combined adult population of 39,773,433, in which 332,868 elective gastroscopies were recorded per year. Overall, this gives a crude national per capita activity rate of 8.4 elective gastroscopy procedures per 1000 adults per year in England **(Figure 4.3)** The practices were ranked nationally according to their age and sex-adjusted annual elective gastroscopy rate and then divided into tertiles (low, medium and high tertiles) as shown in **(Figure 4.4)**. Although most of the results have been presented in relation to these tertile, since this seems a particularly informative approach, the key findings were also justified using other method of exposure in the sensitivity analysis section.

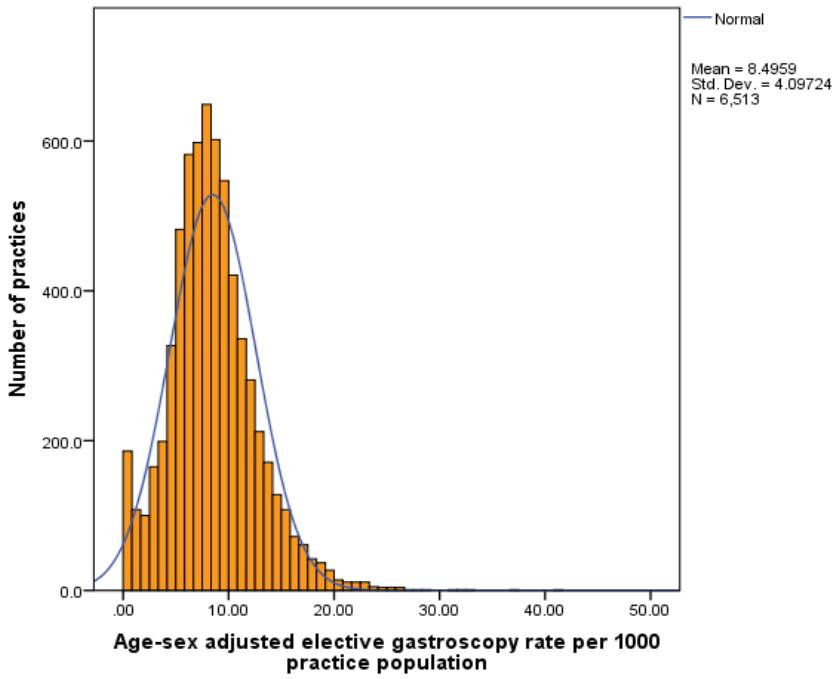


Figure 4.3 Histogram showing the normal distribution of the GP practices according to their age-sex standardized gastroscopy rate per 1000 practice population.

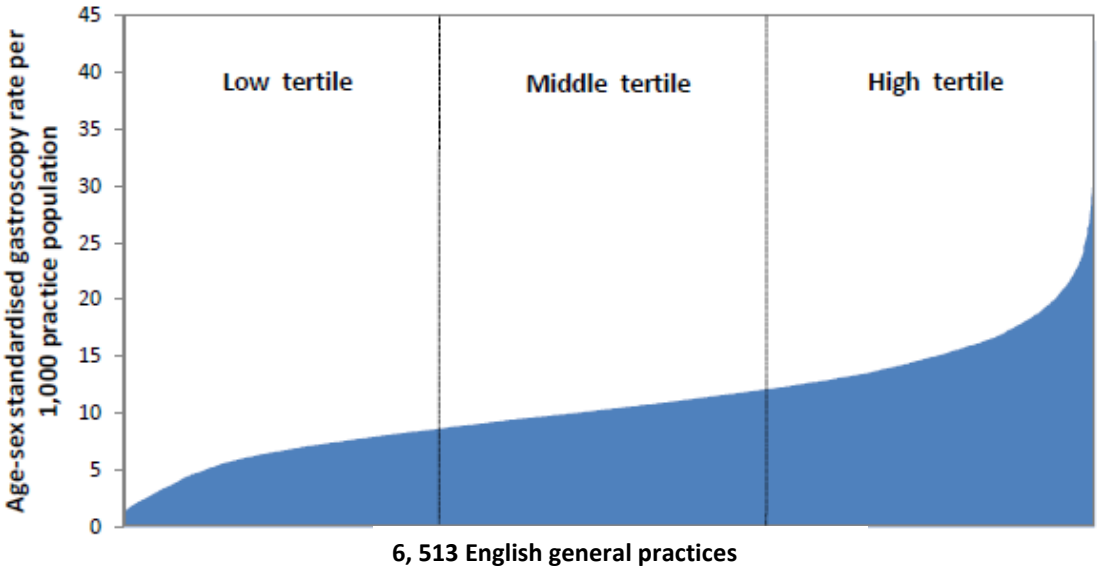


Figure 4.4 GP practices ranked nationally according to their age- and sex-adjusted annual gastroscopy rate and then divided into tertiles (low, medium and high tertiles)

Tertiling of practices by their adjusted elective gastroscopy activity reveals that their mean rate for the high tertile group of practices (12.9 per 1000) was more than 2.5 times (250%) that of practices in the low tertile group (4.4 per 1000) **(Table 4.1)**. The age specific rate for the ≥55 years (Age cut off for gastroscopy referral) of elective gastroscopy procedures performed were also 2.76 times more in high tertile practices. Moreover, it is clear from the table that higher proportions of gastroscopies performed during emergency episodes were coded along with general practices with low rates of elective procedures **(Table 4.1).** It is important to note that over the study period for capturing total elective gastroscopy activity data, 88.2% of the procedures were unique (ie, 'first-time' for individual patients within the 2-year time window). The corresponding figures for each general practice tertile were within 1% of each other (low tertile: 89%; middle tertile: 89%; high tertile 88%).

Table 4.1 The 6,513 General Practices related Gastroscopy procedures number, mode (Elective vs. Emergency) and rates. Results presented overall (total) and grouped into the practice tertiles according to age-sex standardized rate of elective gastroscopy. (HES data: 2006/7-2007/8)

	Total	Low tertile practices	Middle tertile practices	High tertile practices
Number of practices	6513	2171	2171	2171
Registered adult patients	39,773,433	13,634,374	13,861,641	12,277,418
Total annual Gastroscopy (n)	411,175	83,792	141,240	186,143
Elective procedures (n, %)	332,868 (81)	61,137 (73)	114,819 (81)	156,912 (84.3)
Emergency procedures (n, %)	78,307 (19)	22,655 (27)	26,421 (19)	29,231 (15.7)
Average elective gastroscopy rate per 1000 practice population, (SD)				
Crude (Un-adjusted) rate	8.4 (4.2)	4.5 (2)	8.2 (1.4)	12.9 (3.5)
Standardized (Adjusted) rate	8.5 (4.1)	4.4 (1.8)	8.1 (0.8)	12.9 (3.1)
Age specific (≥ 55) rate	16.5 (7.8)	8.9 (4.1)	16.2 (2.5)	24.6 (5.8)

The demographic characteristics of these practices are described in **(Table 4.2).** The populations served by the tertile groups of practices showed no significant differences with respect to age or gender profile. However, there was a significant difference in the distribution of practices with respect to the "average" practice-level deprivation variable (quintile) – the low tertile group contained the lowest proportion of "most deprived" practices whereas the high tertile group contained the highest proportion. Generally, practices within the most socially disadvantaged group illustrated higher rates of gastroscopy. The most affluent group of practices, however, showed the opposite trend. **(Figure 4.5.)**

Table 4.2 Demographic characteristics of 6,513 General Practices in England grouped into tertiles according to their age-sex standardized rate of diagnostic elective gastroscopy.

Characteristic	Total	Low tertile practices (n=2,171)	Middle tertile practices (n=2,171)	High tertile practices (n=2,171)	p value
Adult age groups n,%					
< 55	26,336,483 (66.2)	8,954,744 (65.67)	9,188,880 (66.28)	8,192,859 (66.73)	**Ns**
55 to 64	5,715,513 (14.3)	1,992,359 (14.61)	1,983,889 (14.31)	1,739,265 (14.16)	
65 to 74	4,033,883 (10.1)	1,398,613 (10.25)	1,400,338 (10.10)	1,234,932 (10.05)	
75 to 84	2,649,347 (6.6)	917,894 (6.73)	924,825 (6.67)	806,628 (6.57)	
≥ 85	1,038,207 (2.6)	370,764 (2.71)	363,709 (2.62)	303,734 (2.47)	
Gender					
Male	19,679,660 (49.5)	6,765,876 (49.62)	6,844,554 (49.37)	6,069,230 (49.43)	**Ns**
Female	20,093,773 (50.5)	6,868,498 (50.37)	7,017,087 (50.62)	6,208,188 (50.56)	
Practice deprivation quintile					
Q1 (most deprived)	1,122 (17.2)	243 (11.19)	298 (13.72)	581 (26.76)	<0.001
Q2	1,261 (19.3)	295 (13.58)	410 (18.88)	556 (25.61)	
Q3	1,336 (20.5)	438 (20.17)	438 (20.17)	460 (21.18)	
Q4	1,377 (21.1)	531 (24.45)	502 (23.12)	344 (15.84)	
Q5 (least deprived)	1,417 (21.7)	664 (30.58)	523 (24.09)	230 (10.59)	

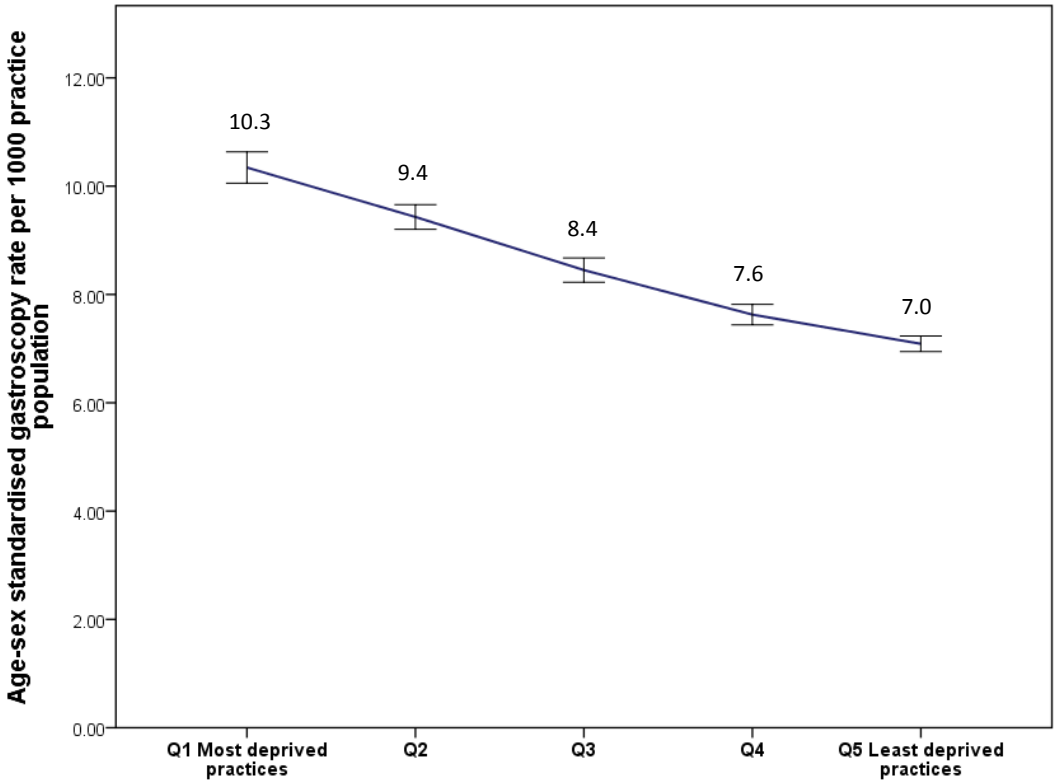


Figure 4.5 The average practices gastroscopy rate with 95% CI distributed according to their level of deprivation.

In addition, practices within the same average deprivation quintile exhibited wide variation in rates of gastroscopy. For example, of these 6,513 included practices, there were 1,222 practices serving the poorest local populations (deprivation quintile 1). For these "deprived" practices, mean adjusted gastroscopy rate was 4.1 per 1,000 for the low tertile group of practices and 13.9 per 1,000 for the high tertile group. Similarly, there were 1,415 practices serving the least deprived populations (quintile 5). For these least deprived practices, the average rate was 4.8 per 1,000 for the low tertile group and 11.4 per 1,000 for the high tertile group of practices **(Figure 4.6).**

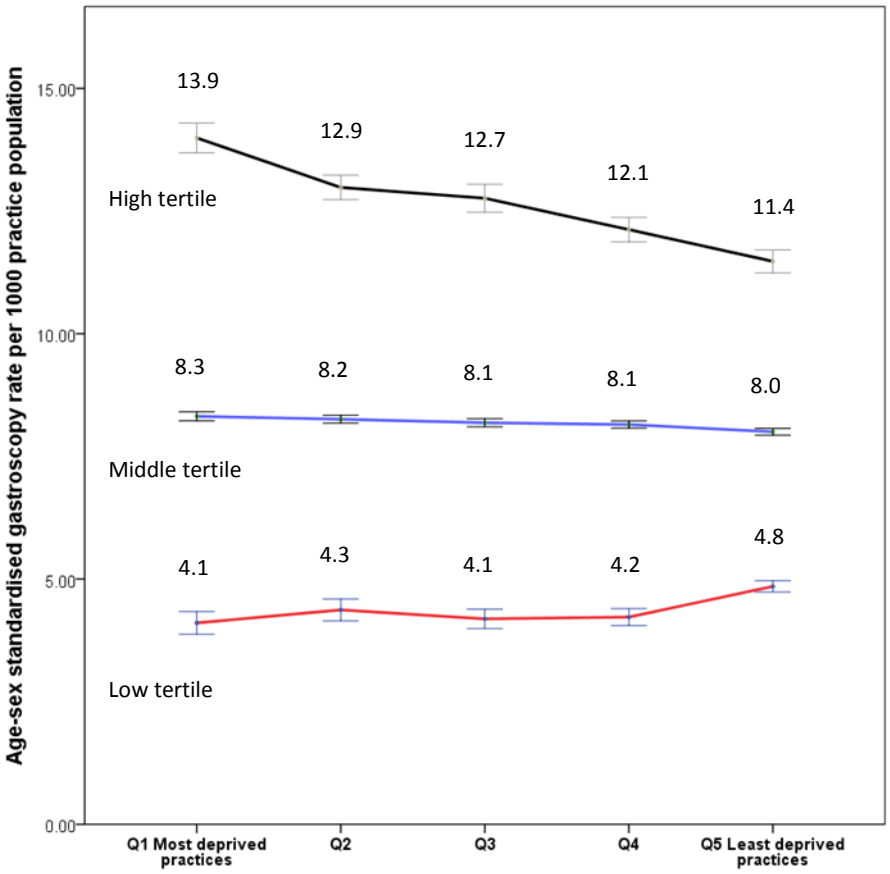


Figure 4.6 shows the age- sex adjusted rate with 95% CI of elective gastroscopy according to the practice level deprivation and across the practice tertile groups.

The strength of such association has further been investigated using linear regression analysis, showing that only 7.9% of variation in age-sex adjusted practice rates is associated with practice-level deprivation (adjusted R-square: 0.079), suggesting that most variation in gastroscopy rates is not accounted for by the average deprivation score of the practice population.

4.5.2 Characteristics of individuals who had elective Gastroscopy procedure across the tertile groups of general practices

587,256 individuals were coded with an elective gastroscopy procedure linked to the 6,513 practices in the study during the 2-year period. The demographic characteristics across the tertile groups of practices for these patients are summarised in **(Table 4.3)**.

There was a small but significant difference in the mean age, with the High tertile group appearing to have younger patients who had this procedure. Again, the distribution of the patients' socioeconomic profile among this tertile was similar to that described in relation to the practices' average deprivation, in which the high tertile group of practices had the highest proportion of "most deprived" patients, and the low tertile group had the highest proportion of "least deprived" patients undergoing gastroscopy.

Table 4.3 The number and demographic characteristics of individuals who had elective gastroscopy at the patient's first elective gastroscopy related hospital episode (across the GP practice terile groups)

	Total	Low tertile practices	Middle tertile practices	High tertile practices	p value
Patients	**587,256**	108,679	203,771	274,806	-
Age, mean (SD) years	59.2 (16.5)	60.2 (16.6)	59.5 (16.5)	58.4 (16.4)	<0.001
Age groups					
< 55	215514 (36.7)	37035 (34.1)	72772 (35.7)	105707 (38.5)	
55 to 64	127237 (21.7)	23321 (21.5)	44014 (21.6)	59902 (21.8)	<0.001
65 to 74	126421 (21.5)	23949 (22.0)	44455 (21.8)	58017 (21.1)	
75 to 84	95628 (16.3)	19440 (17.9)	34238 (16.8)	41950 (15.3)	
≥ 85	22456 (3.8)	4934 (4.5)	8292 (4.1)	9230 (3.4)	
Gender					
Male	263261 (44.8)	49696 (45.7)	91257 (44.8)	122308 (44.5)	Ns
Female	323949 (55.2)	58973 (54.3)	112498 (55.2)	152478 (55.5)	
patients deprivation					
Q1 (Most deprived)	126220 (21.6)	12185 (11.3)	32741 (16.1)	81294 (29.7)	
Q2	118623 (20.3)	16885 (15.6)	40028 (19.7)	61710 (22.5)	<0.001
Q3	119242 (20.4)	21809 (20.2)	43216 (21.3)	54217 (19.8)	
Q4	115317 (19.7)	25698 (23.7)	44208 (21.8)	45411 (16.6)	
Q5 (Least deprived)	105772 (18.1)	31653 (29.2)	42818 (21.1)	31301 (11.4)	

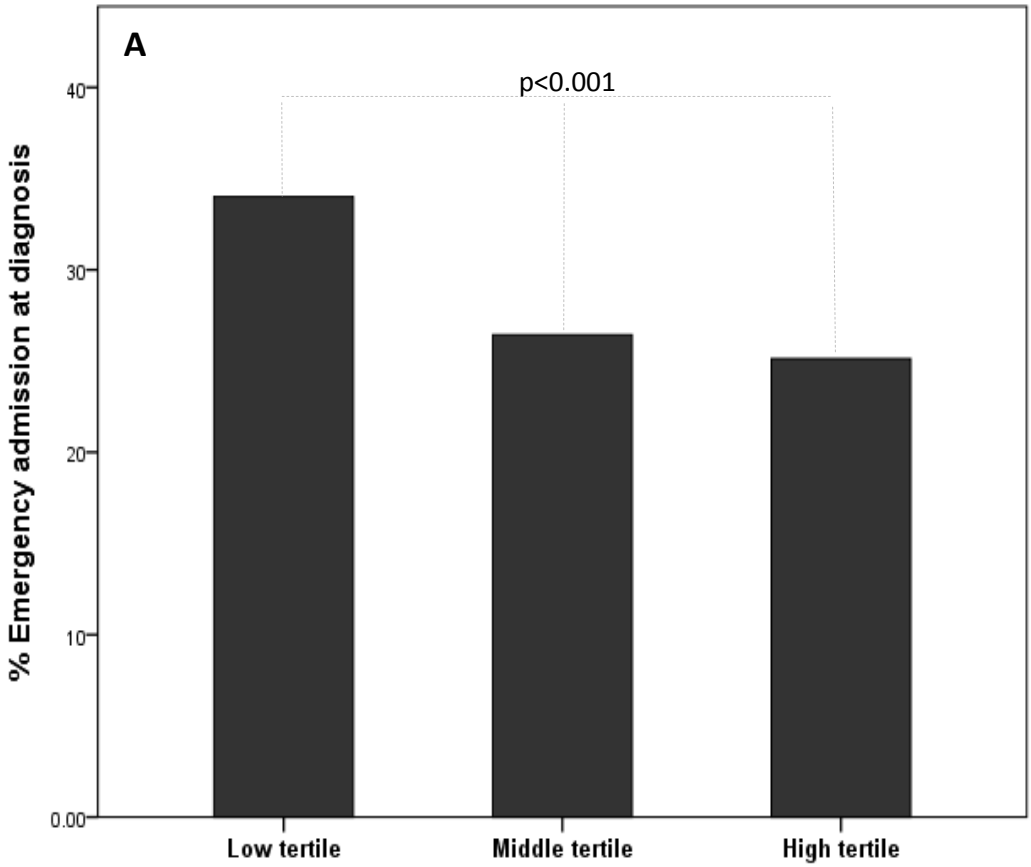
4.5.3 Per capita rate of gastroscopy and OG cancer outcome

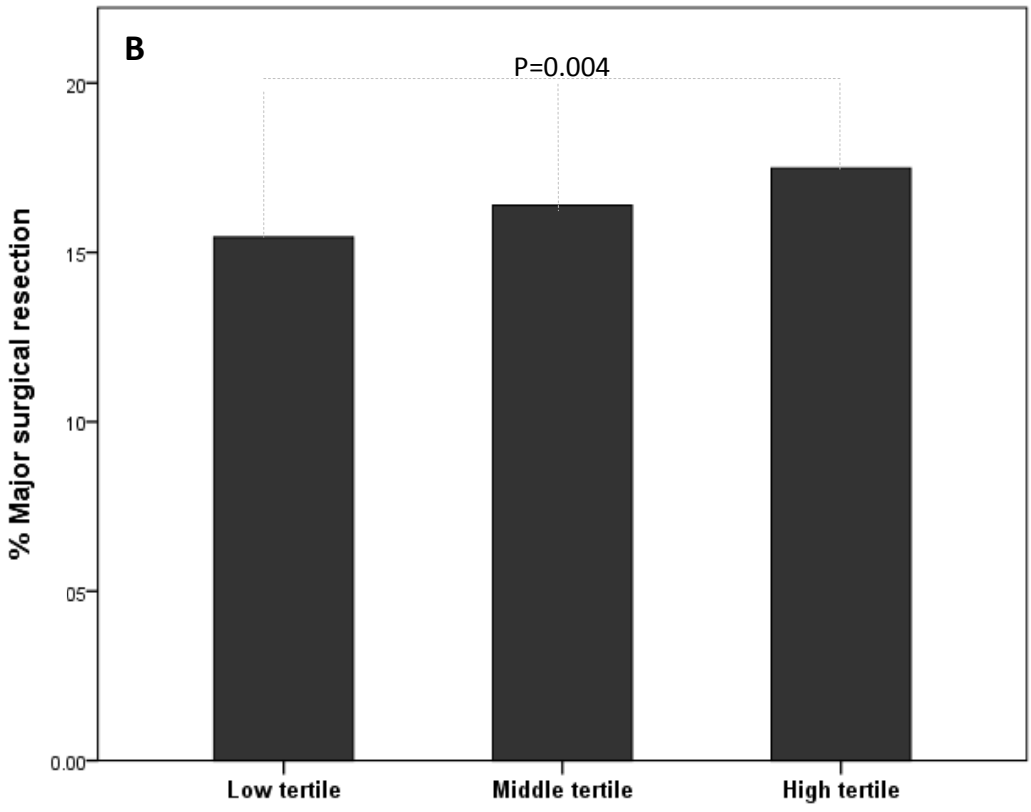
The characteristics of the OG cancer patients by tertile of general practice gastroscopy rate are summarised in **(Table 4.4)**. At the time of index gastroscopy, the average age of cancer patients belonging to practices in the low tertile group was approximately one year older than those belonging to high tertile practices. There was no difference with respect to gender or frequency of co-morbidities across the three groups of practices. The distribution of patient-level deprivation score for the cancer patients across the three practice tertile groups show that the greatest proportion of most deprived cancer patients were in the high tertile group whereas the greater proportion of least deprived cases belonged to the low tertile group of general practices **(Table 4.4)**.

Comparison of crude (unadjusted) outcomes across the tertile showed highly significant differences for all three outcome measures (emergency admission during diagnostic pathway, major surgical resection and mortality within 1-year of index gastroscopy) as shown in **(Figure 4.7)**. Hence, when aggregated nationally, those patients belonging to the low tertile practices (lowest gastroscopy rates) had poorest cancer outcomes. This is despite the fact that overall this group of general practices tended to be serving less deprived practice populations **(Table 4.2)** and had a lower proportion of “most deprived” cancer patients **(Table 4.4)**.

Table 4.4 Characteristics of 22,488 OG cancer patients by tertile of general practice gastroscopy volume (analysis of HES data for England, 2006-2008)

Patient characteristics	Low tertile practices	Middle tertile practices	High tertile practices	P value
Number of cases	6,196	7,913	8,379	-
Age, mean (sd)	72.2 (11.9)	71.6 (11.7)	71.3 (11.6)	0.004
Age groups*				
< 55	508 (8.2)	628 (7.9)	714 (8.5)	
55 to 64	1049 (16.9)	1445 (18.3)	1538 (18.4)	Ns
65 to 74	1672 (27.0)	2255 (28.5)	2415 (28.8)	
75 to 84	2058 (33.2)	2578 (32.6)	2750 (32.8)	
≥ 85	909 (14.7)	1007 (12.7)	962 (11.5)	
Gender				
Male	4045 (65.3)	5239 (66.2)	5517 (65.8)	Ns
Female	2151 (34.7)	2674 (33.8)	2862 (34.2)	Ns
Co-morbidity groups				
1 (No co-morbidity)	4486 (72.4)	5920 (74.8)	6149 (73.4)	Ns
2 (1 co-morbidity)	1112 (17.9)	1344 (17.0)	1508 (18.0)	Ns
3 (2 or more co-morbidity)	598 (9.7)	649 (8.2)	722 (8.6)	Ns
Patient deprivation quintile				
1 (Most deprived)	822 (13.4)	1361 (17.3)	2567 (30.8)	
2	1094 (17.8)	1646 (20.9)	1915 (23.0)	<0.001
3	1275 (20.7)	1700 (21.6)	1636 (19.6)	
4	1470 (23.9)	1671 (21.2)	1344 (16.1)	
5 (Least deprived)	1494 (24.3)	1492 (19.0)	873 (10.5)	


A
p<0.001
% Emergency admission at diagnosis
40
30
20
10
0.00
Low tertile
Middle tertile
High tertile


B
P=0.004
% Major surgical resection
20
15
10
05
0.00
Low tertile
Middle tertile
High tertile

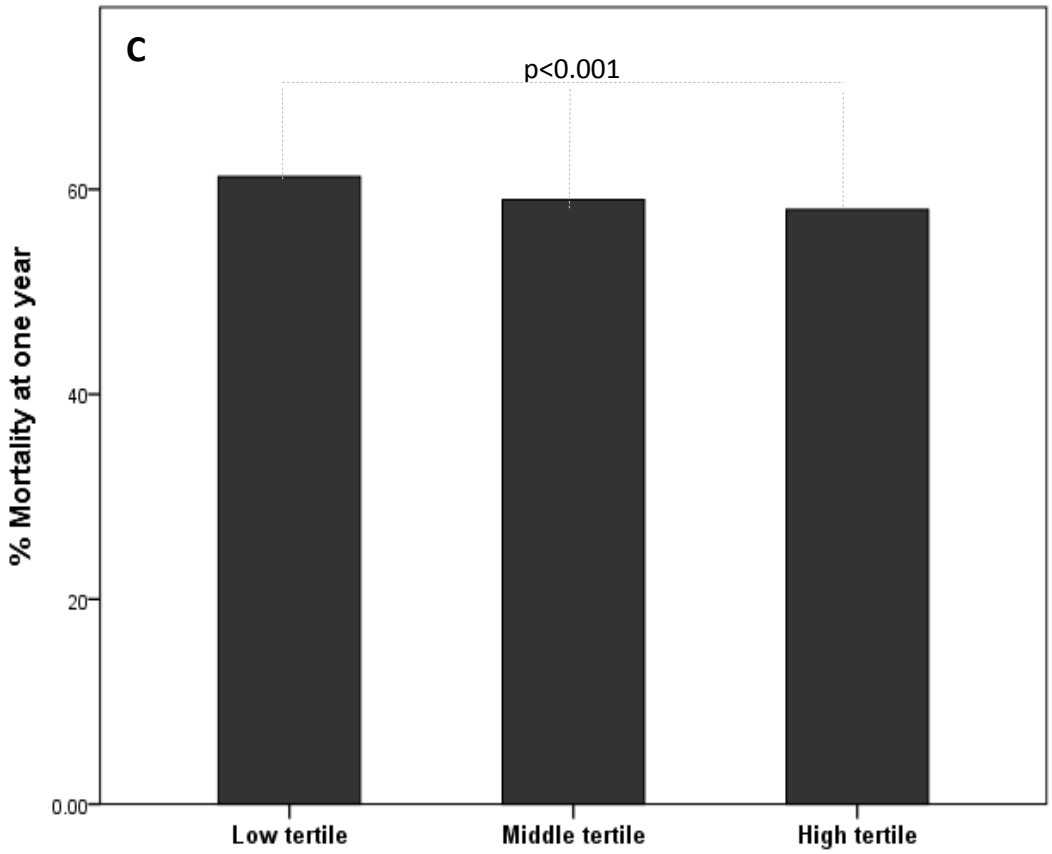
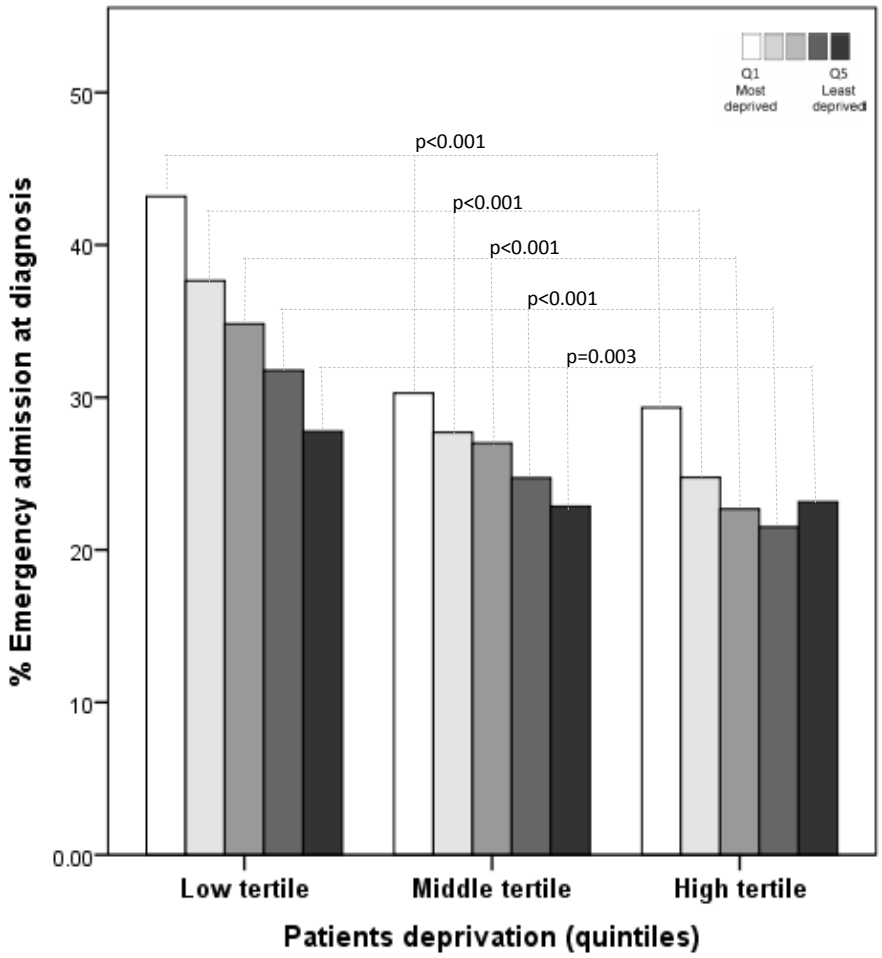


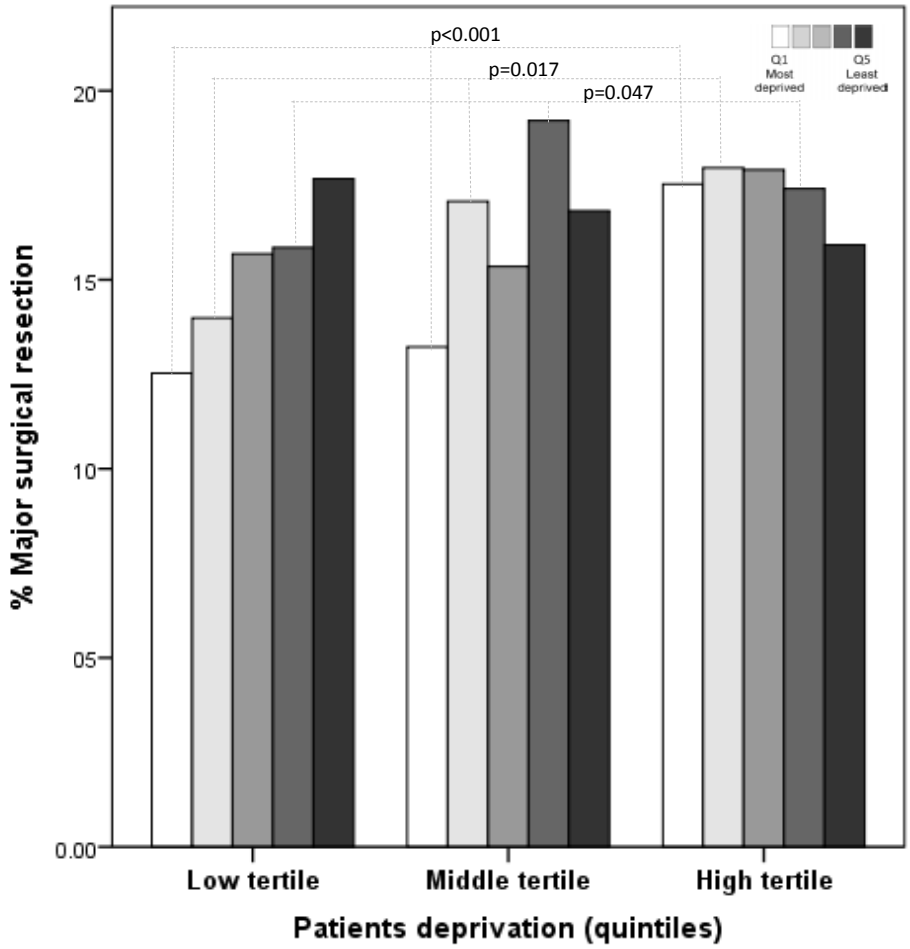
Figure 4.7 Comparison of crude outcomes for OG cancer across the general practice tertile groups (low, middle or high gastroscopy rate per capita). **(A)** Emergency admission during the diagnostic pathway; **(B)** Major surgical resection; **(C)** Mortality at 1 year from index gastroscopy.

Stratified analysis of crude outcomes according to patient-level deprivation **(Figure 4.8, 4.9 and 4.10)** revealed that the imbalance in patient outcome across the three groups of practices was most marked among the most deprived in society (quintile 1). Hence, for the most deprived cases of OG cancer in England, the rate of surgery was just 12.5% for those belonging to low tertile practices, 13.2% for those belonging to medium tertile practices and 17.5% for those registered with a high tertile practice **(**p<0.001; Pearson Chi-square; **Figure 4.8)**. Similar trends were apparent for the other outcomes **(Figure 4.9 and Figure 4.10)**.



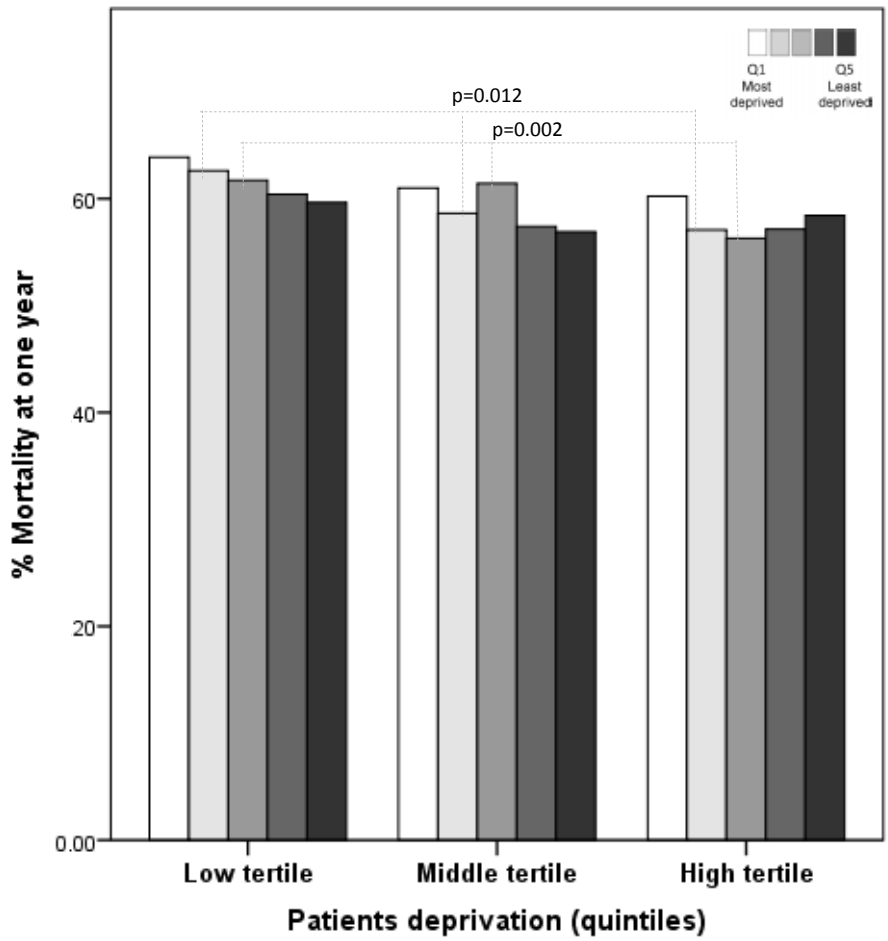
2	412/1094 **(37.6 %)**	456/1646 **(27.7 %)**	474/1915 **(24.7 %)**	<0.001
3	444/1275 **(34.8 %)**	459/1700 **(27.0 %)**	371/1636 **(22.7 %)**	<0.001
4	467/1470 **(31.7 %)**	413/1671 **(24.7 %)**	289/1344 **(21.5 %)**	<0.001
5 (Least deprived)	415/1494 **(27.7 %)**	341/1492 **(22.8 %)**	202/873 **(23.1 %)**	0.003

Figure 4.8 Crude (unadjusted) rate of emergency admission as a route of diagnosis of OG cancer patients according to general practice tertile for gastroscopy rate (low, middle or high): Stratified for deprivation quintile of the patient based on their individual LSOA code. Quintile 1 refers to patients living in the most socioeconomically deprived areas of England.



OG cancer patients deprivation group	Low tertile	Middle tertile	High tertile	P value
1 (Most deprived)	103/822 **(12.5 %)**	180/1361 **(13.2 %)**	450/2567 **(17.5 %)**	0.001
2	153/1094 **(13.9 %)**	281/1646 **(17.1 %)**	344/1915 **(17.9 %)**	0.016
3	200/1275 **(15.7 %)**	261/1700 **(15.3 %)**	293/1636 **(17.9 %)**	n/s
4	233/1470 **(15.8 %)**	321/1671 **(19.2 %)**	234/1344 **(17.4 %)**	0.047
5 (Least deprived)	264/1494 **(17.7 %)**	251/1492 **(16.8 %)**	139/873 **(15.9 %)**	n/s

Figure 4.9 Crude (unadjusted) rate of major surgical resection for OG cancer patients according to general practice tertile for gastroscopy rate (low, middle or high): Stratified for deprivation quintile of the patient based on their individual LSOA code. Quintile 1 refers to patients living in the most socioeconomically deprived areas of England.



OG cancer patients deprivation group	Low tertile	Middle tertile	High tertile	P value
1 (Most deprived)	525/822 **(63.8 %)**	830/1361 **(60.9 %)**	1546/2567 **(60.2 %)**	n/s
2	685/1094 **(62.6 %)**	965/1646 **(58.6 %)**	1093/1915 **(57.1 %)**	0.012
3	787/1275 **(61.7 %)**	1044/1700 **(61.4 %)**	921/1636 **(56.3 %)**	0.002
4	888/1470 **(60.4 %)**	959/1671 **(57.4 %)**	768/1344 **(57.1 %)**	n/s
5 (Least deprived)	891/1494 **(59.6 %)**	849/1492 **(56.9 %)**	510/873 **(58.4 %)**	n/s

Figure 4.10 Crude (unadjusted) mortality at 12 months for OG cancer patients according to general practice tertile for gastroscopy rate (low, middle or high): Stratified for deprivation quintile of the patient based on their individual LSOA code. Quintile 1 refers to patients living in the most socioeconomically deprived areas of England.

Finally, we performed multiple logistic regression analysis to identify factors associated with each of the three cancer outcomes after adjustment for potentially confounding co-variates. This confirmed independent associations between poorer cancer outcomes and advancing age, increased co-morbidity and patient deprivation quintile **(Tables 4.5, 4.6** and **4.7)**. As expected, poorer patient deprivation status was associated with worse outcomes. The general practice (average) deprivation quintile was an independent predictor only for emergency admission.

Consistent with our hypothesis, we found that the exposure of interest (general practice gastroscopy rate tertile) was a significant and independent predictor for all three cancer outcome variables. Hence, after adjustment for age, co-morbidity and deprivation, there were highly significant associations between cancer outcomes and the general practice rate of gastroscopy. Compared to patients belonging to practices in the highest tertile, those in the lowest gastroscopy rate tertile were 1.73 times as likely to be admitted as an emergency during the diagnostic pathway **(Table 4.5)**, 0.87 times as likely to undergo major surgical resection **(Table 4.6)** and 1.14 times as likely to be dead within 12 months of gastroscopy **(Table 4.7)**.

Table 4.5 Factors associated with emergency admission during diagnostic pathway in patients with OG cancer in England (n=22,488). Unadjusted and adjusted odds ratios with 95% CI based on univariate and multivariate logistic regression (Reference group = 1)

Variable	n,%	Unadjusted (univariate)			Adjusted (multivariate)		
		OR	CI	p value	OR	CI	p value
Age group							
< 55	421/1850 (22.75)	**1**	-	-	**1**	-	-
55 to 64	752/4032 (18.65)	0.77	0.68-0.89	<0.001	0.82	0.71-0.95	0.01
65 to 74	1434/6342 (22.61)	0.99	0.87-1.12	0.895	1.03	0.90-1.18	0.62
75 to 84	2375/7386 (32.15)	1.60	1.42-1.81	<0.001	1.69	1.49-1.92	<0.001
≥ 85	1322/2878 (45.93)	2.88	2.53-3.28	<0.001	3.30	2.87-3.80	<0.001
Gender							
Female	2352/7687 (30.59)	**1**	-	-	**1**	-	-
Male	3952/14801 (26.7)	0.82	0.77-0.87	<0.001	0.93	0.87-0.99	0.033
Co-morbidity groups							
No co-morbidity	3361/16555 (20.3)	**1**	-	-	**1**	-	-
1 co-morbidity	1728/3964 (43.59)	3.03	2.81-3.26	<0.001	2.95	2.74-3.19	<0.001
≥ 2 co-morbidities	1215/1969 (61.7)	6.32	5.73-6.98	<0.001	6.85	6.19-7.58	<0.001
Practice deprivation							
1 Most deprived	1020/3215 (31.72)	**1**	-	-	**1**	-	-
2	1283/4415 (29.06)	0.88	0.79-0.97	0.012	0.84	0.76-0.94	0.004
3	1389/4923 (28.21)	0.84	0.76-0.93	0.001	0.84	0.74-0.94	0.004
4	1334/5001 (26.67)	0.78	0.71-0.86	<0.001	0.79	0.70-0.90	<0.001
5 Least deprived	1278/4934 (25.9)	0.75	0.68-0.83	<0.001	0.75	0.66-0.86	<0.001
Patient deprivation [a]							
1 Most deprived	1520/4750 (32)	**1**	-	-	**1**	-	-
2	1342/4655 (28.82)	0.86	0.78-0.94	0.001	0.86	0.78-0.96	0.006
3	1274/4611 (27.62)	0.81	0.74-0.88	<0.001	0.80	0.71-0.89	<0.001
4	1169/4485 (26.06)	0.74	0.68-0.82	<0.001	0.74	0.66-0.84	<0.001
5 Least deprived	958/3859 (24.82)	0.70	0.63-0.77	<0.001	0.68	0.59-0.78	<0.001
Practice gastroscopy rate tertile							
High	2105/8379 (25.12)	**1**	-	-	**1**	-	-
Middle	2092/7913 (26.43)	1.07	0.99-1.14	0.055	1.19	1.10-1.29	<0.001
Low	2107/6196 (34)	1.53	1.42-1.65	<0.001	1.73	1.60-1.88	<0.001

[a] Excluding 128 (0.6%) with missing deprivation score

Table 4.6 Factors associated with chance for major surgical resection in patients with OG cancer in England (n=22,488). Unadjusted and adjusted odds ratios with 95% CI based on univariate and multivariate logistic regression (Reference group = 1)

Variable	n,%	Unadjusted (univariate)			Adjusted (multivariate)		
		OR	CI	p value	OR	CI	p value
Age group							
< 55	491/1850 (26.54)	**1**	-	-	**1**	-	-
55 to 64	994/4032 (24.65)	0.90	0.79-1.02	0.122	0.86	0.75-0.97	0.023
65 to 74	1371/6342 (21.61)	0.76	0.67-0.86	<0.001	0.72	0.64-0.81	<0.001
75 to 84	806/7386 (10.91)	0.33	0.29-0.38	<0.001	0.31	0.28-0.36	<0.001
≥ 85	57/2878 (1.98)	0.05	0.04-0.07	<0.001	0.05	0.03-0.06	<0.001
Gender							
Female	1129/7687 (14.68)	**1**	-	-	**1**	-	-
Male	2590/14801 (17.49)	1.23	1.14-1.32	<0.001	n/s	n/s	n/s
Co-morbidity groups							
No co-morbidity	2944/16555 (17.78)	**1**	-	-	**1**	-	-
1 co-morbidity	689/3964 (17.38)	0.97	0.88-1.06	0.552	1.09	0.99-1.20	0.070
≥ 2 co-morbidity	86/1969 (4.36)	0.21	0.16-0.26	<0.001	0.20	0.16-0.25	<0.001
Practice deprivation							
1 Most deprived	567/3215 (17.63)	**1**	-	-	**1**	-	-
2	725/4415 (16.42)	n/s	n/s	n/s	n/s	n/s	n/s
3	795/4923 (16.14)	n/s	n/s	n/s	n/s	n/s	n/s
4	814/5001 (16.27)	n/s	n/s	n/s	n/s	n/s	n/s
5 Least deprived	818/4934 (16.57)	n/s	n/s	n/s	n/s	n/s	n/s
Patient deprivation							
1 Most deprived	733/4750 (15.43)	**1**	-	-	**1**	-	-
2	778/4655 (16.71)	n/s	n/s	n/s	1.15	1.02-1.29	0.015
3	754/4611 (16.35)	n/s	n/s	n/s	1.20	1.07-1.35	0.001
4	788/4485 (17.56)	n/s	n/s	n/s	1.32	1.17-1.48	<0.001
5 Least deprived	654/3859 (16.94)	n/s	n/s	n/s	1.28	1.13-1.44	<0.001
Practice gastroscopy rate tertile							
High	1465/8379 (17.48)	**1**	-	-	**1**	-	-
Middle	1297/7913 (16.39)	0.92	0.85-1.01	0.063	0.90	0.82-0.98	0.019
Low	957/6196 (15.44)	0.86	0.78-0.94	0.001	0.87	0.79-0.95	0.004

Table 4.7 Factors associated with 12 month mortality in patients with OG cancer in England (n=22,488). Unadjusted and adjusted odds ratios with 95% CI based on univariate and multivariate logistic regression (Reference group = 1)

Variable	n, %	Unadjusted (univariate)			Adjusted (multivariate)		
		OR	CI	p value	OR	CI	p value
Age group							
< 55	874/1850 (47.24)	**1**	-	-	**1**	-	-
55 to 64	1964/4032 (48.71)	1.06	0.95-1.18	0.296	1.10	0.99-1.24	0.075
65 to 74	3385/6342 (53.37)	1.27	1.15-1.41	<0.001	1.33	1.20-1.48	<0.001
75 to 84	4867/7386 (65.89)	2.15	1.94-2.39	<0.001	2.26	2.03-2.51	<0.001
≥ 85	2232/2878 (77.55)	3.85	3.40-4.37	<0.001	4.13	3.63-4.70	<0.001
Gender							
Female	4695/7687 (61.07)	**1**	-	-	**1**	-	-
Male	8627/14801 (58.28)	0.89	0.84-0.94	<0.001	n/s	n/s	n/s
Co-morbidity groups							
No co-morbidity	9295/16555 (56.14)	**1**	-	-	**1**	-	-
1 co-morbidity	2421/3964 (61.07)	1.22	1.14-1.31	<0.001	1.14	1.06-1.22	<0.001
≥ 2 co-morbidity	1606/1969 (81.56)	3.45	3.07-3.88	<0.001	3.61	3.20-4.07	<0.001
Practice deprivation							
1 Most deprived	1890/3215 (58.78)	**1**	-	-	**1**	-	-
2	2652/4415 (60.06)	n/s	n/s	n/s	n/s	n/s	n/s
3	2909/4923 (59.08)	n/s	n/s	n/s	n/s	n/s	n/s
4	2959/5001 (59.16)	n/s	n/s	n/s	n/s	n/s	n/s
5 Least deprived	2912/4934 (59.01)	n/s	n/s	n/s	n/s	n/s	n/s
Patient deprivation							
1 Most deprived	2901/4750 (61.07)	**1**	-	-	**1**	-	-
2	2743/4655 (58.92)	0.91	0.84-0.99	0.034	0.88	0.81-0.96	0.006
3	2752/4611 (59.68)	0.94	0.86-1.02	0.169	0.87	0.80-0.95	0.002
4	2615/4485 (58.3)	0.89	0.82-0.96	0.007	0.82	0.75-0.89	<0.001
5 Least deprived	2250/3859 (58.3)	0.89	0.81-0.97	0.009	0.81	0.74-0.89	<0.001
Practice gastroscopy rate tertile							
High	4861/8379 (58.01)	**1**	-	-	**1**	-	-
Middle	4667/7913 (58.97)	1.04	0.97-1.10	0.212	1.06	0.99-1.13	0.056
Low	3794/6196 (61.23)	1.14	1.06-1.22	<0.001	1.14	1.06-1.22	<0.001

4.5.4 Sensitivity analyses

To further confirm the association between the practice gastroscopy rate and cancer outcome, additional multivariate analyses using different "exposure" variables were used to express the gastroscopy rate of the patient's general practice. In all cases, these analyses confirmed the independent association between gastroscopy rate at the general practice and all three cancer outcomes after adjustment for confounders **(Figures 4.11-4.14)**.

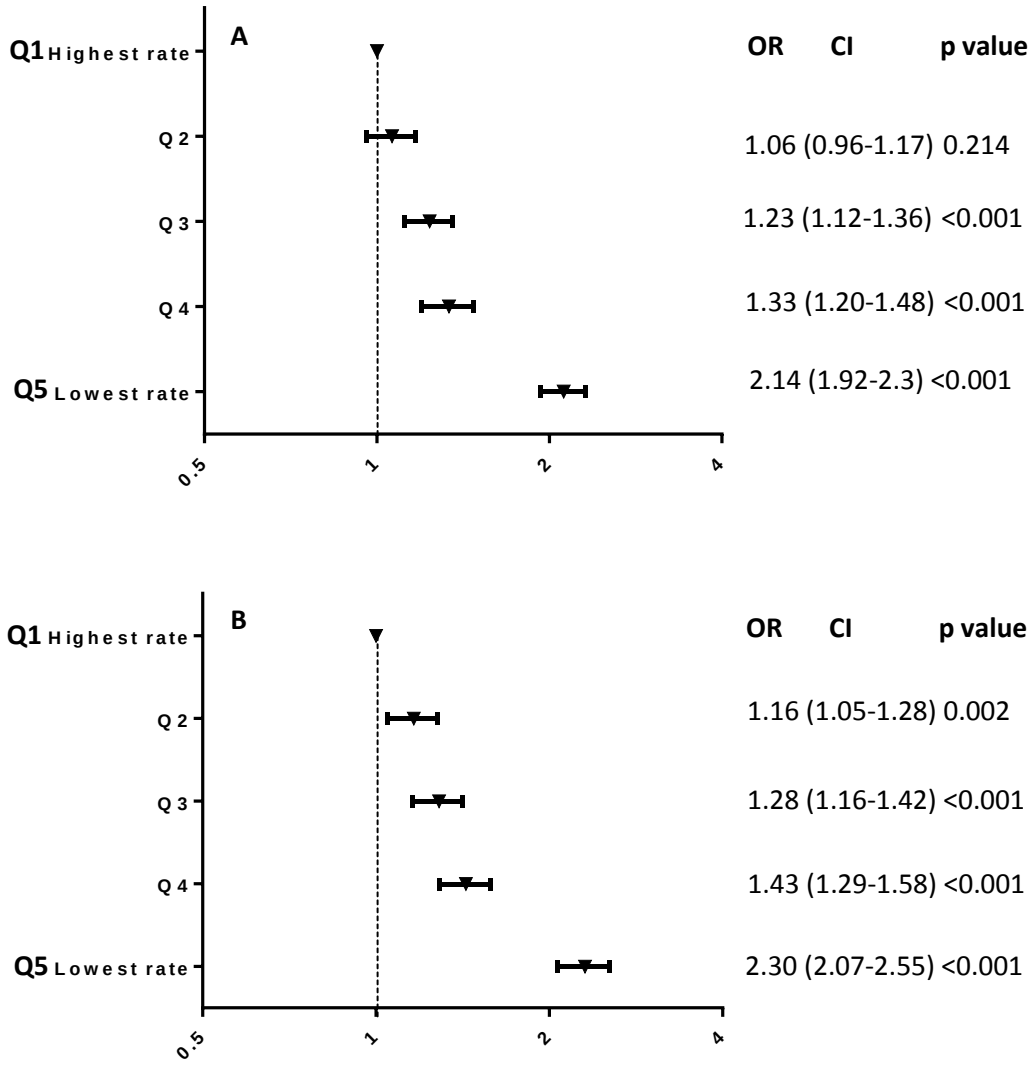


Figure 4.11 Sensitivity analyses showing the association between general practice elective gastroscopy rates and emergency route of diagnosis for 22,488 cases of OG cancer. Logistic regression (multi-variate) analysis using (A) Quintile of adjusted elective gastroscopy rate, and (B) Quintile of age-specific rate (>55 years) where Quintile 1 refers to the Highest.

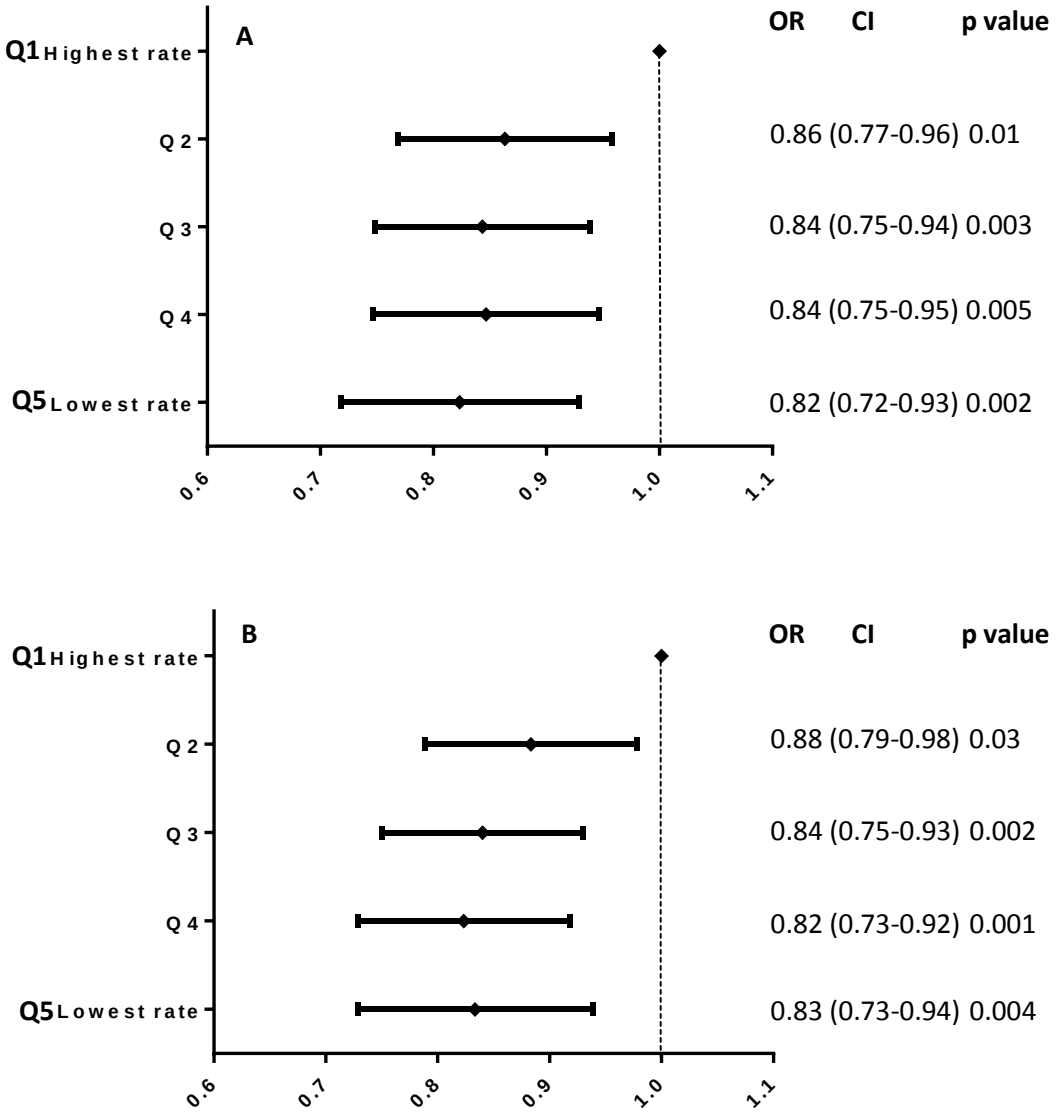


Figure 4.12 Sensitivity analyses showing the association between general practice elective gastroscopy rates and major surgical resection for 22,488 cases of OG cancer. Logistic regression (multi-variate) analysis using (A) Quintile of adjusted elective gastroscopy rate, and (B) Quintile of age-specific rate (>55 years) where Quintile 1 refers to the Highest.

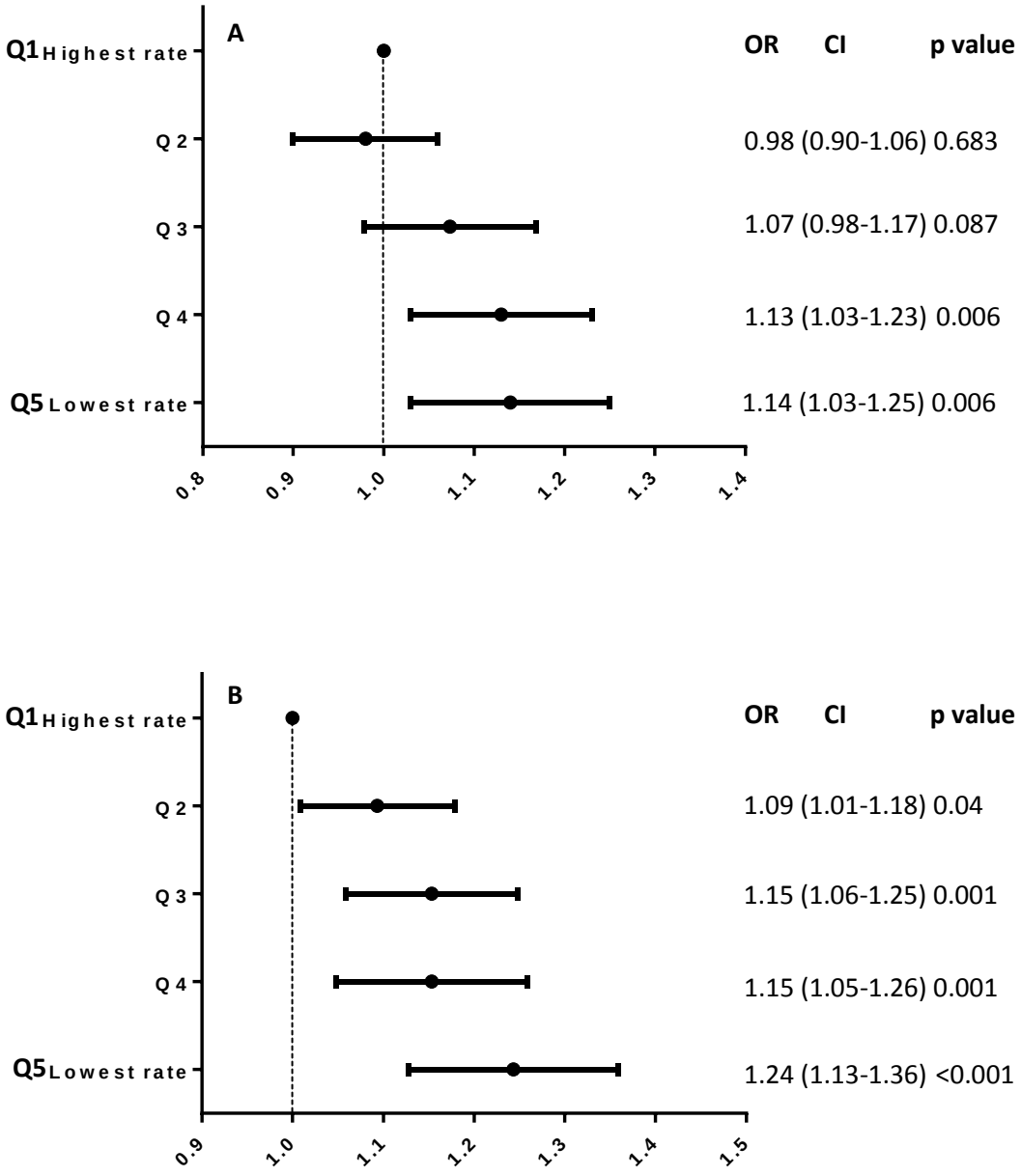


Figure 4.13 Sensitivity analyses showing the association between general practice elective gastroscopy rates and mortality at 12 month for 22,488 cases of OG cancer. Logistic regression (multi-variate) analysis using (A) Quintile of adjusted elective gastroscopy rate, and (B) Quintile of age-specific rate (>55 years) where Quintile 1 refers to the Highest.

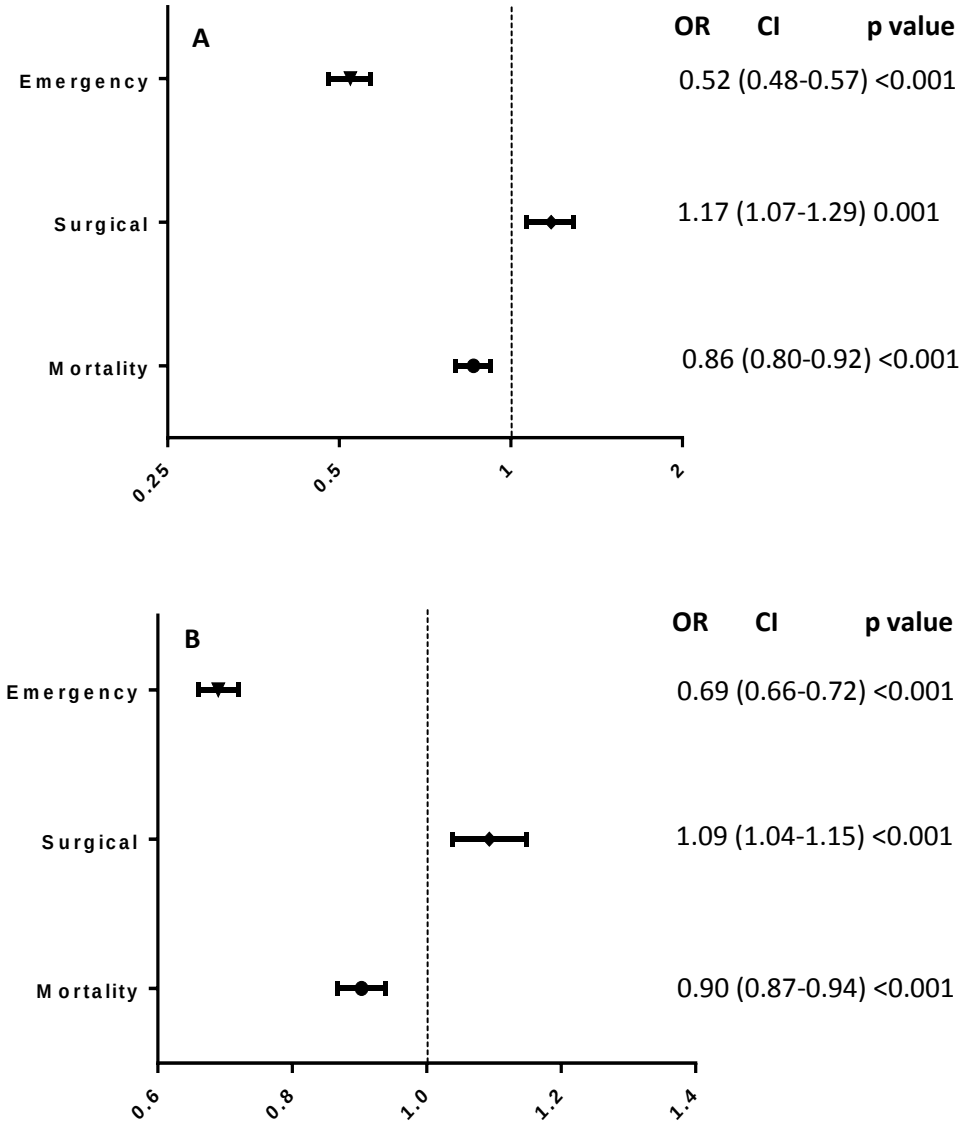


Figure 4.14 Sensitivity analyses confirming association between general practice elective gastroscopy rates and emergency route of diagnosis, major surgical resection and death at 12 month for 22 488 cases of OG cancer. Logistic regression (multi-variate) analysis using continuous variable for (A) actual age-sex-adjusted elective gastroscopy rate of the patient's general practice (expressed as rate per 100 population) and (B) continuous variable for actual age-specific rate for adults >55 years of age. The OR represents the change in odds per unit increase in gastroscopy rate (eg, an increase from 1 per 100 to 2 per 100 practice population per year).

4.6 Discussion

This chapter has confirmed the wide variability in per capita rates of elective gastroscopy at the level of general practice populations. This variation does not appear to be explained by simple demographics factors in keeping with the published literature. [185] With regard to the NICE clinical guideline age related cut-off for gastroscopy referral, this study measures not only the crude and adjusted gastroscopy rate but also explored the age specific rate among patients aged 55 years and above, which further emphasises the wider variation between tertiles.

Although practices serving populations in more deprived areas were more likely to have higher rates of gastroscopy, there was no simple relationship between gastroscopy rates and socioeconomic status, and most variation appears unexplained by this factor. Further research is therefore required to understand the causes for practice-level variation in gastroscopy rates.

To our knowledge, this is the first study examining the association between primary care gastroscopy rates and cancer outcome, albeit the need for research in this area has been highlighted.[164] Consistent with our main hypothesis, we found that cancer outcomes were significantly different for patients belonging to practices with low, medium or high gastroscopy rates. After adjusting for confounding variables, we found that patients diagnosed from a practice within the lowest tertile of gastroscopy rate were significantly less likely to undergo major surgery than those from a practice in the highest tertile.

Inequality in outcome was most divergent for cancer patients from the lowest deprivation category. Similar trends of inequality in the rate of emergency

admission and all-cause mortality within a year of gastroscopy were apparent. These data provide strong evidence for an independent association between OG cancer outcomes and gastroscopy rates at the local practice level. It is interesting to note that across the tertiles of practices (low through medium to high), there is a very small but significant trend for lower mean age of cancer patients at the time of index gastroscopy this would be consistent with a trend towards earlier diagnosis in areas exposed to higher rates of gastroscopy.

These findings do not imply that individual general practices with low or high rates of gastroscopy are exhibiting poor or good practice, nor that low rates are always associated with worse outcomes. It is not possible from routine data to judge whether the level of gastroscopy at an individual practice is 'appropriately' low or high. However, our study suggests that populations that are exposed to lower rates of investigation appear, on average, to experience worse cancer outcomes. It is of particularly concern that patients belonging to the most disadvantaged socioeconomic category have the greatest inequality in cancer outcomes with respect to practice gastroscopy rates.

As expected, socioeconomic deprivation was found to be an independent predictor of poor cancer outcomes for OG tumours—this phenomenon has been described for a range of cancers.[77, 268, 311]

In this part of the study, general practices belonging to the low tertile for gastroscopy rate are, on average, serving more affluent populations, and have the lowest proportion of cancer patients from the most disadvantaged areas. Hence, the inferior outcomes for this group of 'low-referring' practices, overall, cannot be

explained by a confounding influence of deprivation. Our stratified analyses for deprivation illustrate a potential reason for this paradox—socially disadvantaged patients who are registered with a low referring practice have particularly poor outcomes (the worst in the country). This suggests that a 'low' gastroscopy rate is a potential indicator that might be used to identify practices where doctors may wish to review their referral policies, particularly in more deprived areas, where practice gastroscopy rates tend to be higher.

Strengths of this study include the utilization of patient population data that allowed us to test our hypothesis on a national scale with the benefit of large numbers. This part of the project captures gastroscopy procedures coded in HES across 2006-2008 data years. The extracted elective procedures were not filtered by diagnostic field, and therefore they include both patients who were subsequently diagnosed with cancer and those who were not subsequently coded with cancer. These procedures were summed for persons registered at each general practice as coded in the national data, and only practices with incident OG cancer cases within the same data years (as described in chapter 3) were included in the final analysis. Furthermore, we undertook extensive sensitivity analyses using a range of approaches to quantify the exposure of interest, and found the findings to be robust.

Our national gastroscopy rate in general population is 8.4 per 1000 populations per annum, matching the previously reported BSG figure of 8.6 in 1992 and 10.0 per 1000 in 2001.[146] The 2007 NICE commissioning guidance of upper GI endoscopy service reported that the average referral rate was 5.4 per 1000 per year based on

the prevalence of alarm symptoms through the rapid access services and 7.5 per 1000 per year if patients were referred by the standard open access service.[149] This NICE guidance also reports that the average (directly standardized) rate of this procedure was 9.5 per 1000 per year according to the analysis of data that was collected by the Information Centre as part of the hospital episode statistics 2004-2007 returns.[149]

The benchmarked indirect standardization method was used in our study to measure the practices' adjusted gastroscopy rates which showed almost no difference with the observed crude rates at either national or tertile level. This suggests that there are no major discrepancies in the age and sex profiles between these practices. Generally, this small effect of standardization for age, sex and social class on the variation in the referral rate for general practices has been well reported in the previous literature. [201] Wilkin and Smith, for example, concluded that there are similar proportions of patients at each age, gender and social class group that had referral; however, high referrers were referring more patients in each category.[312]

This study presents the national elective gastroscopy activity data for more than 2000 GP practices in each tertile within a 2 year time window, and therefore any apparent variation is highly unlikely to be affected by the fact that random variation in the number of referrals could be due to chance. Such issue was previously reported by various studies as a result of their small number of included referral and the short period of data collection. [201, 313]

Certainly, this analysis like any other ecological or observational study accepts that it can be at risk of 'ecological fallacy' and cannot adjust for all possible confounders. [314] Thus this study makes no claim that our findings of such association between per-capita gastroscopy rate and OG cancer outcome necessarily proves causality. [314]

While it is essential to acknowledge that some data discrepancies are inevitable, it is unlikely that these have systematically biased the results in favour of the hypothesis. This chapter has reported the great care taken to explore potential bias in our approach to data aggregation through the undertaking of extensive sensitivity analyses. Each case of OG cancer was assigned a range of alternative variables to express the gastroscopy rate at the patient's local practice.[314, 315] Hence, instead of expressing the rate as tertile groups alone, we examined quintiles, continuous variables (i.e. the absolute rate for each individual practice) and age-specific rates for patients over 55 years old.[314, 315] This meant re-assigning practices and their relative ranking across a range of scenarios, to produce alternative patient-level exposure variables. We studied not one but three measures of cancer outcome in patient-level binary logistic regression analyses.[314, 315] Although we cannot exclude ecological fallacy, the remarkable consistency of our results gives weight to our findings. [314, 315]

Although there was a significant difference in the distribution of practices with respect to the practice-level deprivation variable, at the same time, all tertile groups contained practices from every deprivation quintile. Additionally, general practices serving populations with the same average deprivation score exhibited a

wide spectrum of gastroscopy rates, after adjusting for age and sex profile. The magnitude of such association was further explored by linear regression analysis, which is shown to be at less than 8%. Hence deprivation status provides little effect on the variation observed.

This analysis did not adjust for possible variation between hospitals in cancer treatment outcome, since this was not a likely confounder given our study design and the selected outcome measures. The emergency admission during diagnostic pathway, for instance, is a surrogate marker for diagnostic delay or failure of elective referral. This outcome will not be influenced by the quality of the local hospital treatment after diagnosis. Similarly, the rate of major surgical resection is unquestionably reflective of earlier diagnosis, since only patients with an early stage disease will be candidates for potentially curative resection. Neither of these outcome variables is relevant to subsequent post-diagnostic management at the local hospital.

Whilst the one year mortality after index gastroscopy will be dictated largely by cancer stage at the time of diagnosis and it is certainly plausible that institutional-level variations in staging investigations, treatment quality and surgical volume may impact on survival rates [127], nevertheless the majority of patients with OG cancer tend to be diagnosed at a late and incurable stage. Our overall cancer mortality statistic is therefore unlikely to be influenced significantly by this phenomenon.

In a climate of cost restraint in the UK national health system, there is an inevitable and reasonable focus on identifying and constraining ‘excessive’ use of secondary

care investigations. [315] Local initiatives aimed at reducing gastroscopy activity may well avoid unnecessary investigations for younger patients with benign disease without compromising clinical outcome. [315] However, analysis of the findings from this study suggest that there is a pressing need to focus on both ends of the referral volume spectrum. [315]

Chapter 5 Variation in elective gastroscopy rates in English general practice populations: Is there evidence to suggest different thresholds for referral between practices?

5.1 Introduction

In the UK, general practice is the key mode for delivering primary health care to the resident population. Each practice contains one or more family doctors who usually work with a practice manager, nurses and other associated health professionals such as health visitors, all of whom are responsible for the care of patients registered on their list.

The Royal College of General Practitioners (RCGP) define primary care as:

'…the first level contact with people taking action to improve health in a community. In a system with a gatekeeper, all initial (non-emergency) consultations with doctors, nurses or other health staff'.

With almost 300 million general practice consultations per year, general practice is for most people the first and most commonly used way of accessing the NHS.[310, 316]

Generally, variations in referral rates from primary care level generalists to more specialised secondary care services have been a long-standing clinical and economic concern.[185, 186, 205, 206] As noted in Chapter 1, dyspepsia is a very common reason for people to visit their GP, accounting for 3-4% of all consultations [317]. Serious underlying disease is rare and the typical GP (serving approximately 2,000 patients) may see only one to two new case of upper gastrointestinal cancer per year. [10] UK general practitioners fulfil an important gatekeeper role in selecting dyspeptic patients for upper GI endoscopy, and they are encouraged to adhere to NICE guidelines [147, 148, 213]. A key focus of these guidelines is the empirical (symptom-based) treatment of dyspepsia including non-invasive strategies (*H.*

pylori 'test-and-treat') and early gastroscopy is advocated mainly for those with suspected cancer on the basis of 'alarm' or 'red flag' features. However, the poor sensitivity and specificity of alarm features for diagnosis of upper GI cancers is acknowledged. [87, 88, 94]

Hence, GPs face a challenging task. On the one hand, a 'gate-keeper' role is mandated by NICE guidelines, and it is a role that seeks to restrict 'over-investigation' of benign symptoms. On the other, the identification of cancer cases by 'alarm symptoms' alone remains unreliable, so that the majority of cases are diagnosed at a late and incurable stage. Other symptoms might predict O-G cancer, but with absolute risks of about 1 %.[91] This makes for a dilemma in distinguishing patients with dyspepsia manageable at GP level from the minority who need referral to specialist care or diagnostic gastroscopy.

A fast-track system for investigation of patients with alarm features (under the 'two week rule') was implemented under the National Cancer Plan. [108] Although promoted as an attempt to improve the number of early-stage cancers detected, numerous studies have shown that the adoption of this pathway has produced little improvement in the detection of curable cancer. [164, 173, 176] This is consistent with the concern that the 'alarm' features identified as triggers to fast-track referral are often features of more advanced disease.

Moreover, for various tumour types there is evidence that patients identified by GPs as having 'suspected cancer' may fall outside the strict national referral criteria and yet do indeed have an underlying malignancy [147, 148, 213-215]. Baughan et

al (2011) suggest that there may be additional factors that lead to clinical suspicion of cancer but that do not satisfy simplistic referral rules.[216, 318]

Expert opinion from primary care has expressed concern that:

"… GPs are being forced to 'manipulate' the two-week cancer pathway by inflexible NICE referral criteria that make no allowances for their 'sixth sense' " [319]

There are further suggestions that:

"There is good evidence that there is a terrific variation in the way GPs use the two-week pathway. What we see is that some practices use it a lot, but relatively few of these patients have cancer. Other practices use it very little, but most of the patients referred have cancer"…."What matters is not really how many patients you refer, but how many of those patients are diagnosed with cancer. We would like to see a high detection rate through the two-week wait pathway." [319]

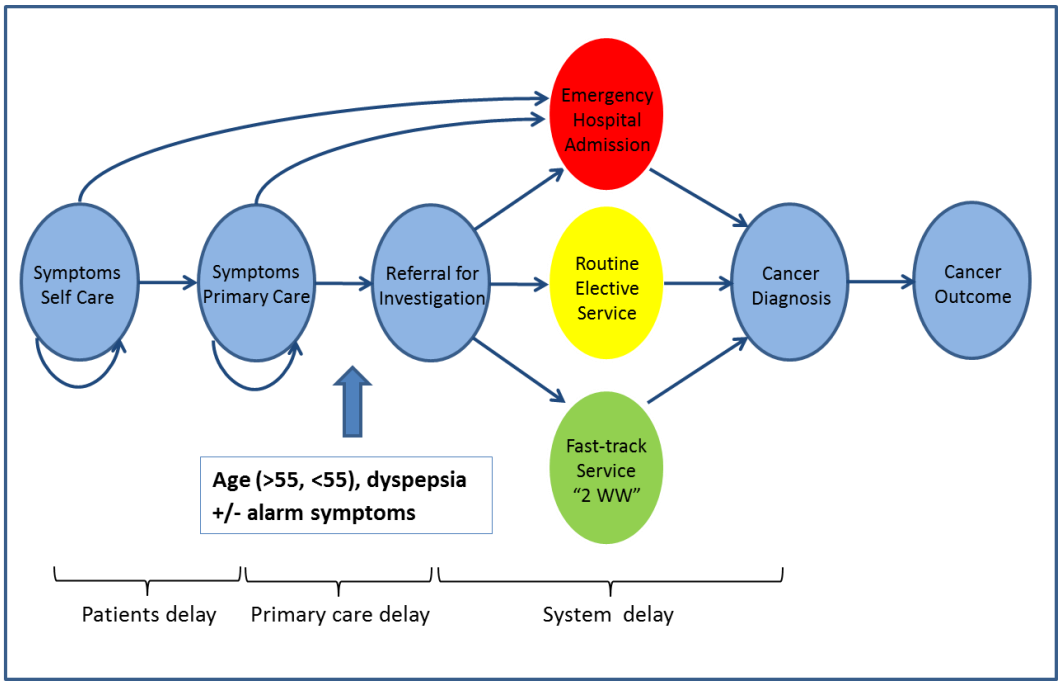


Figure 5.1 OG cancer patients' pathway of care, routes of diagnosis and possible level of delayed diagnosis.

Variation in thresholds for gastroscopy referral is an entirely expected phenomenon given the controversy that exists regarding the correct placement of this investigation in the management of upper gastrointestinal symptoms.[320]

In chapter 4, evidence was presented to show an association between variations in rates of elective gastroscopy at the level of general practice populations, and outcomes for oesophago-gastric cancer.[315] Specifically, we have found that low rates are associated with risk of poorer outcome. We have shown also that deprivation explains only a small proportion (less that 8 %) of the observed variation in gastroscopy rates. Further studies are presented in the present chapter to test the idea that wide variation in rates of gastroscopy between practices is reflective (at least to some extent) of genuine differences in clinical 'threshold' for referral. We postulated that practices with relatively low rates of gastrosopy may be operating more selective referral policies, thereby reserving gastroscopy for older patients and/or those with more severe symptoms (e.g. alarm symptoms). If so, it should be possible to find evidence for a difference in the age distribution and 'diagnostic yield' (proportion of patients with serious pathology) among patients referred for gastroscopy from 'low referring' practices.

The work described in this chapter also seeks to confirm the phenomenon of 'small area' variation in gastroscopy rates between general practices that are situated in close geographical proximity. The factors that determine rates of gastroscopy for general practices across the country are likely to be complex, and variation in clinical practice is clearly but one of several factors. It was not possible to control for differences in local symptom prevalence, consultation behaviour or variable

access to local secondary care diagnostics in our national study. However, the demonstration of wide variation in referral rates within a small geographical area would lend support to the notion that practice rates are 'unexplained' by such confounders and that a key determinant of variation must be differences in referral practice.

Finally, we wished to examine the possible association at practice level between overall rates of referral under the two week rule for all cancer types and the rate of gastroscopy. The assumption underlying such association was to test whether practices with low gastroscopy rates are also low in their use of the two week wait system in general – an association that could support the idea of generalised differences in referral behaviour.

5.2 Aims and objectives

This chapter aims to provide evidence to support the idea that there are different thresholds for referral between general practices in England. Such a hypothesis could (at least in part) explain the very wide variation we have observed in per capita gastroscopy rates in general practice populations

Using both national and local audit data, the studies described in this final part of the thesis aim to show:

1) That the demographic and clinical pattern of patients undergoing elective gastroscopy from low, middle and high referring practices is compatible with differences in referral threshold. Hence, practices with low gastroscopy

rates would be expected to refer older patients (on average) and have a higher yield of serious pathology.

2) That wide variation in per capita gastroscopy rates can be demonstrated within small geographical areas and even adjacent practices, where it is reasonable to assume relatively consistent symptom burden and cultural-behavioural factors relating to consultation.

Aims (1) and (2) will be tested first in national (HES) data. Then, an independent local study will seek to confirm these observations using locally-derived data from one hospital centre and focussing on practices referring exclusively to this centre. This study eliminates any potential confounding influence of variation in secondary care provision or access to gastroscopy.

3) Whether there is an association between practice level elective gastroscopy rate and the per capita rate of total referrals under the 'two week wait' (TWW) for cancers in general. The prediction here is for there to be a positive correlation between these measures, reflecting a common 'referral threshold' factor. Hence, low users of fast-track cancer services in general might be expected to have relatively low rates of gastroscopy.

5.3 Method

5.3.1 Gastroscopy procedure diagnostic profile

5.3.1.1 National diagnostic profile

A key requirement was development of a methodology for categorising the coded diagnoses recorded for all elective gastroscopy procedures. A very wide selection of ICD-10 diagnostic codes are available for encoding gastroscopy episodes and a classification system was needed to allocate patients into logical baskets of conditions.

Using the previously described elective gastroscopy procedure dataset (containing all procedures coded in HES for the GP practices in the study, 2006-2008 **(chapter 4)**, a method was designed to allocate diagnosis codes at the primary position of the patients' first gastroscopy and cluster these diagnoses into six groups as follows:

1. Upper GI cancer (C15-C16 codes)
2. Major acid peptic disease.
3. Normal or minor pathologies.
4. Other GI neoplasm.
5. Upper GI symptoms codes only.
6. Miscellaneous.

Subsequently, the same grouping of codes was undertaken across all other diagnostic positions. An algorithm was then developed to apply a hierarchy system to allocate each gastroscopy to the most 'serious' category recoded. This reflects the fact that several codes (including the use of symptom codes at position 1) may be recorded to describe the endoscopy findings. This involved a ranking (Group 1

being the highest and Group 6 the lowest rank). For example; if any coding position (DIAG 1-14) contained an ICD-10 code for OG cancer (Group 1), then this patient was labelled with an upper GI cancer diagnosis. This avoided mislabelling a cancer case if a symptom code (e.g. Dysphagia) or complication of cancer (e.g. oesophageal stricture, unspecified) was recorded in position 1 above the cancer diagnosis. Similarly, if a patient had a code from Group 2 (Major acid-peptic lesions) at any position, then this patient was categorized as a Group 2 unless there was an OG cancer code recorded (Group 1). This process was repeated until group 6 (Miscellaneous) where patients have no code related to any other higher ranked group from position 1 to 14.

5.3.1.2 Local diagnostic profile (analysis of routine local endoscopy datasets)

Elective gastroscopy procedures performed locally at Aintree University Hospital (Liverpool, UK) in the period between April 2009 and March 2012 were identified using the endoscopy reporting tool (Unisoft). Each endoscopy report was linked to the individual patient's GP practice. Practices with a known population list size and demographics were selected. An inclusion criterion was that each practice in the study was confirmed as referring predominantly to our centre, based on examining the profile of coded gastroscopies recorded in our HES dataset. Hence, all **63** practices in the study were verified as having at least 90% of all their elective gastroscopy procedures coded at our Trust (PROCODE: **REM**) during 2006-2008. As described previously **(Chapter 2)**, the age-sex adjusted elective gastroscopy rates were calculated but using the locally recorded gastroscopy counts taken from the

hospital reporting tool. Practices were ranked and divided into local tertiles (21 practices each).

The local hospital reporting tool contains a greater clinical depth of information than was available from national HES data. Hence, in the local study the gastroscopy reports in Unisoft were analysed to obtain information about endoscopic indication **(Figures 5.2)** in addition to the categorising of endoscopy findings **(Figure 5.3)**. These characteristics were studied first by route of referral (two week wait vs. other elective routes) and then across the local tertile of practices' gastroscopy rate. Sub-analysis was also carried out for those fast tracking patients who were deemed to be at higher risk of cancer. At Aintree University Hospital, this service is known as RAUGICS (Rapid Access Upper GI Cancer Service).

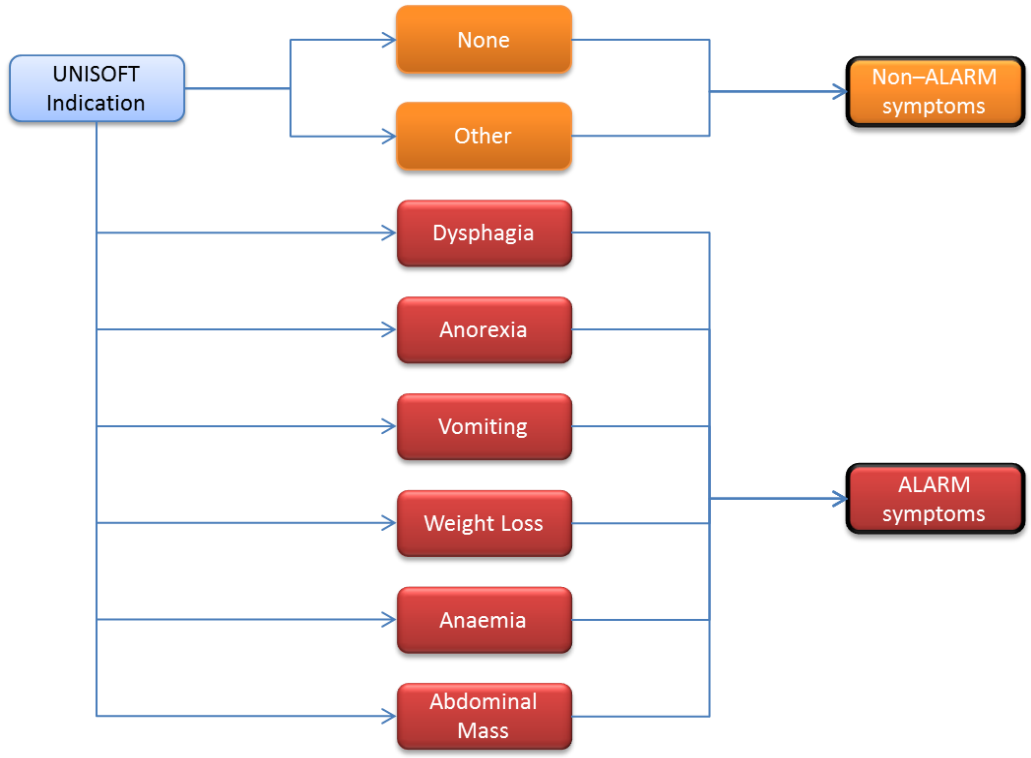


Figure 5.2 System used in the local study for categorising referral indication (symptom profile) based on information recorded in the endoscopy reporting system (UNISOFT).

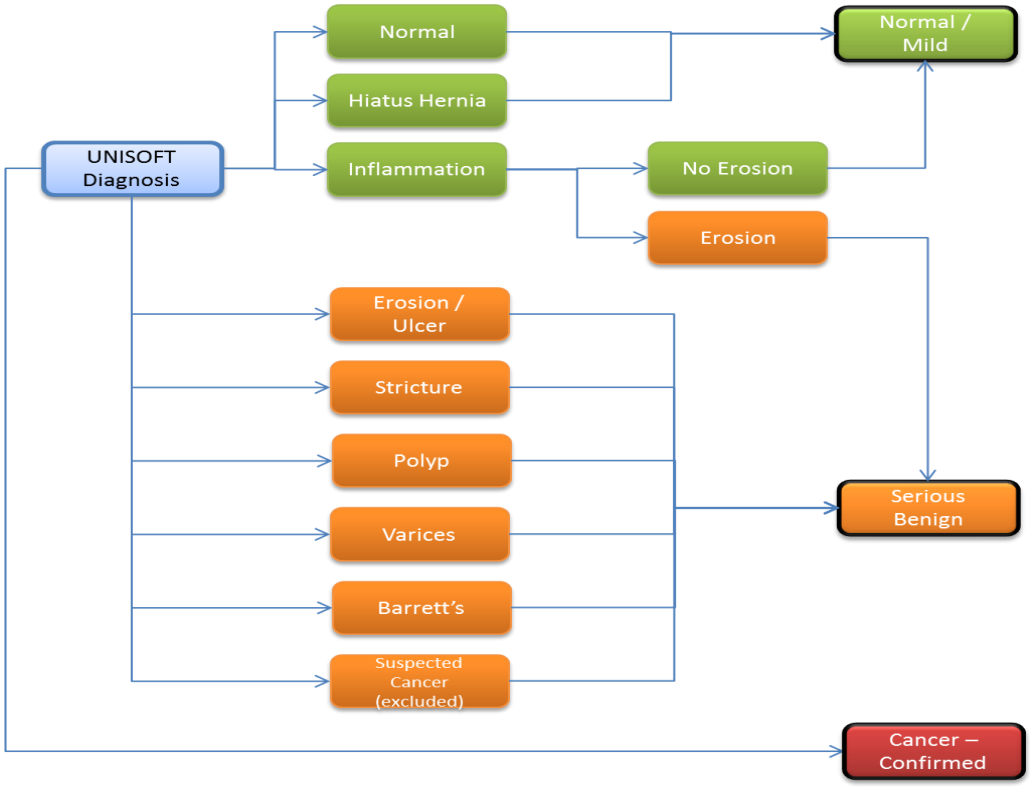


Figure 5.3 System used in the local study for categorising diagnosis profile of gastroscopy procedures as recorded in the UNISOFT reporting tool.

5.3.2 Small area variation in gastroscopy rate across general practices

5.3.2.1 National HES data: Intra-PCT variation in practice rates of gastroscopy

Firstly, we aimed to describe the range of variation in general practice gastroscopy rates *within* individual primary care trusts (PCTs) in England. During the study period, the general practices in the study (n=6513) were grouped administratively and geographically into PCTs responsible for commissioning services from their local hospitals. For each individual PCT (n=152), we determined the absolute range of adjusted gastroscopy rate for the study practices (lowest to highest rate) and calculated the magnitude of variation across the local PCT range. Practices within a single PCT will share common local referral pathways and guidelines and will have access to the same local hospital secondary care services.

5.3.2.2 Local database study: Geographical mapping of local general practices

To further establish evidence for small area variation in practice gastroscopy rates, we adopted a geographical mapping technique to seek examples of practices with wide differences in gastroscopy rate but in very close geographical proximity. Using general practice postcode data provided by the Health and Social Care Information Centre (HSCIC) [321], followed by manual verification, we generated a spreadsheet of postcode data for each general practice included in the local study (n=**63**). The practices were then mapped using public domain mapping software (Google Fusion Tables) [322] and were colour coded for gastroscopy rate per capita, according to their tertiles distribution (low, middle and high groups). The resulting map provides a visual illustration of geographical location of practices.

5.3.3 Associations between practice level gastroscopy rate and the rate of two week wait referrals for any form of cancer

5.3.3.1 National data

External data from the National Cancer Intelligence Network (NCIN) were obtained for the study practices. The dataset contains age-adjusted rates of two week wait (TWW) referrals for any suspected cancer (i.e. all types). [323] The correlation between overall rates of TWW referrals and rates of adjusted gastroscopy rates (derived from HES) were examined. Analyses were further stratified for practices deprivation status (by quintiles) to explore the potential influence of socioeconomic deprivation.

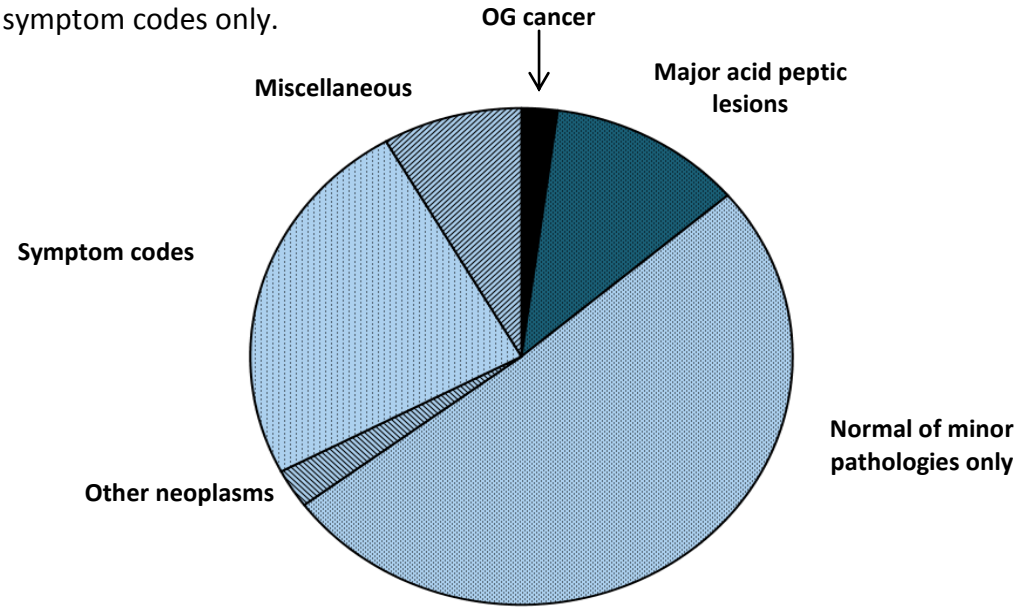
5.3.3.2 Local data

Similarly, correlations between practice population rates of gastroscopy and of TWW referrals in general were examined using the local datasets. The local gastroscopy dataset allowed elective gastroscopies to be categorised as fast-track (TWW) or not. This information is not encoded in the national (HES) datasets but was available in the endoscopy reporting system. For the local practices, this allowed the study of 'fast-track' referrals alone and the calculation of the percentage of all gastroscopy procedures performed via the TWW system (i.e. the number of upper GI endoscopies performed via TWW route divided by the total number of elective gastroscopies).

5.4 Results

5.4.1 National diagnostic profile and comparison across practice tertiles

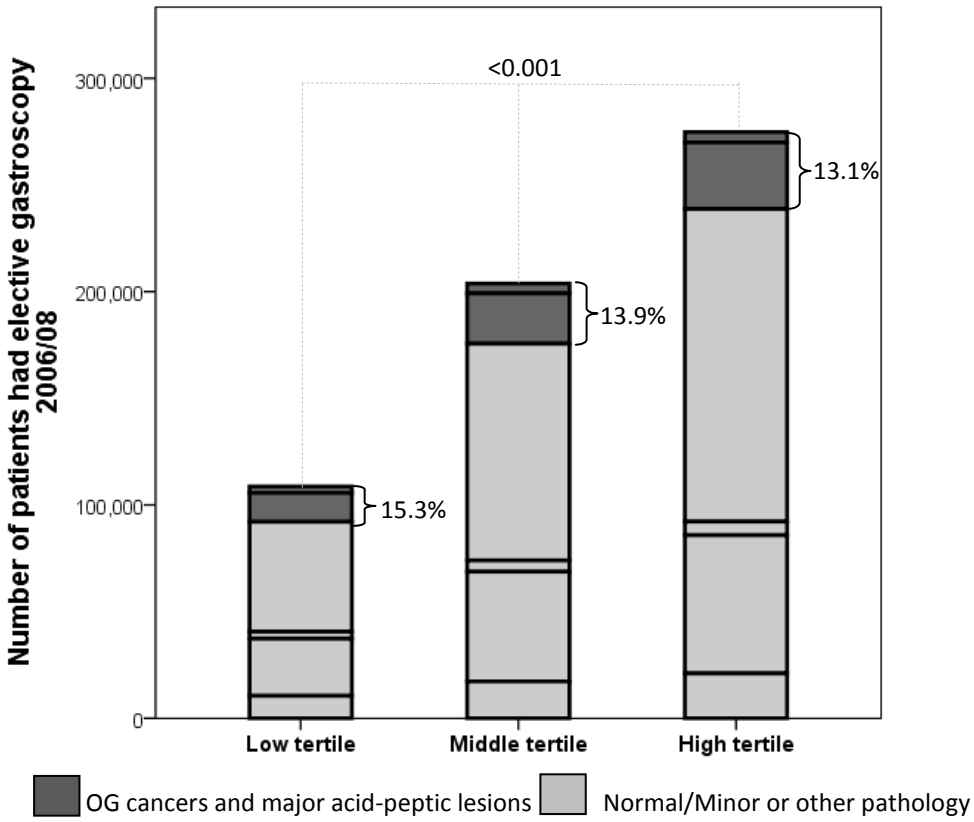
Nationally, the diagnostic profile of individual patients at their first elective gastroscopy related hospital episodes during the data period is demonstrated in **(Figure 5.4)**. Upper gastrointestinal malignancy accounts for only 2.1% of all patients undergoing investigation. Other major acid-peptic lesions (e.g. peptic ulcers) account for a further 11.6% of people undergoing the procedure. The remaining 86.2% of gastroscopies are coded mainly with minor pathologies or with symptom codes only.



Patients had elective gastroscopy for all reasons	
Patients, n	587,256
Age (Mean, SD)	59.2 (16.5)
Patients diagnosis profile	
Upper GI cancer	12569 (2.1)
Major acid-peptic lesions	68229 (11.6)
Normal or minor	299706 (51.0)
Other neoplasms	14920 (2.5)
Symptom codes only	142955 (24.3)
Miscellaneous codes	48877 (8.3)

Figure 5.4 Total number of individual patients undergoing elective upper GI endoscopy in England (2006-2008) and the diagnostic profile based on categorisation of coded diagnoses

Comparison of diagnostic profiles among patients referred for gastroscopy procedures across the practice gastroscopy rate tertiles **(Figure 5.5)** reveals a higher proportion of serious pathology in the low tertile group (cancers and major acid-peptic lesions; $p<0.001$, Chi Square test). To be precise, in relation to the total number of patients who had gastroscopy in each tertile, high referring practices appear to have more patients coded with normal or minor gastroscopy findings, while within the low tertile practice population, there were more patients allocated to more serious pathologies. Furthermore, the mean age of patients referred for gastroscopy was highest for low tertile practices **(Table in lower panel of Figure 5.5)**. This pattern of slightly older age and higher yield of serious pathology among 'low referring' practices is consistent with a more selective or restrictive approach to gastroscopy.



Patients had elective gastroscopy for all reasons	Low tertile practices	Middle tertile practices	High tertile practices	p value
Patients, n	108,679	203,771	274,806	-
Age (Mean, SD)	60.2 (16.6)	59.5 (16.5)	58.4 (16.4)	<0.001
Patients diagnosis profile				
Upper GI cancer (C15,C16)	3025 (2.8)	4612 (2.3)	4932 (1.8)	
Major acid-peptic lesions	13570 (12.5)	23565 (11.6)	31094 (11.3)	
Normal or minor pathologies	51516 (47.4)	101609 (49.9)	146581 (53.3)	<0.001
Other neoplasms	3224 (3.0)	5283 (2.6)	6413 (2.3)	
Symptom codes only	26768 (24.6)	51440 (25.2)	64747 (23.6)	
Miscellaneous codes	10576 (9.7)	17262 (8.5)	21039 (7.7)	

Figure 5.5 Number of individuals undergoing upper GI endoscopy across the GP practice tertile groups and their spectrum of coded diagnoses

5.4.2 Local (Aintree University Hospital) Gastroscopy activity:

Information relating to 13,082 elective gastroscopy cases was collected locally. Of these, 4,003 (30.6%) procedures were through the fast-track (TWW) referral pathway, known locally as RAUGICS (Rapid Access Upper GI Cancer Service) **(Table 5.1)**. As expected, on average the patients referred via RAUGICS were older than for other elective routes reflecting the age cut-off of 55 years for those without alarm symptoms. It is also clear from this table that the fast-track system was used mainly to investigate patients who predominantly (76.5%) referred with alarm symptoms. As expected, a higher "yield" for cancer diagnosis was observed among patients referred though the two week wait system.

Table 5.1 Demographics, referral indication (symptom profile) and diagnostic profile for 13,082 local individuals who underwent elective (non-emergency) gastroscopy. Data are presented overall (total elective) and categorised according to "fast-track" (RAUGICS) or other routes.

	Total elective	**RAUGICS**	**Other elective**	**p value**
Number of patients	13082	4003 (30.6)	9079 (69.4)	
Age, **Mean (SD)**	56 (17)	60 (16)	55 (17)	<0.001
Over 55 **n,%**	7272 (55.6)	2630 (65.7)	4642(51.1)	<0.001
Under 55 **n,%**	5810 (44.4)	1373 (34.3)	4437 (48.9)	
Gender				
Female **n,%**	7364 (56.3)	2332 (58.3)	5032 (55.4)	0.003
Male **n,%**	5718 (43.7)	1671 (41.7)	4047 (44.6)	
Symptoms profile				
ALARM symptoms **n,%**	6266 (47.9)	3062 (76.5)	3204 (35.3)	<0.001
Non- Alarm symptoms, including Isolated dyspepsia **n,%**	6816 (52.1)	941 (23.5)	5875 (64.7)	
Diagnosis profile				
OG cancer **n,%**	182 (1.4)	95 (2.4)	87 (1.0)	<0.001
Serious Benign **n,%**	3907 (29.9)	1182 (29.5)	2725 (30.0)	n/s
Normal or Mild **n,%**	8993 (68.7)	2726(68.1)	6267 (69.0)	n/s

Analysis of patient profiles according to the local practice gastroscopy tertiles shows wide variation in rates of elective gastroscopy between practice populations served by the same local hospital (>2 fold difference in mean rate between low and high groups, as shown in **(Table 5.2)**. Consistent with the national picture based on coded diagnoses extracted from HES data, our analysis of diagnoses recorded in the local gastroscopy reporting system demonstrates that practices with low rates of gastroscopy tend to have a higher "diagnostic yield" of serious pathology and slightly older patients referred for investigation. In additional, the local profile shows that low tertile practices had a higher proportion of patients investigated with alarm or red-flag symptoms than the other practice groups. This provides further evidence for an association between low rates of gastroscopy in the practice population and a higher threshold for referral. The above trends were maintained among patients who had their diagnostic procedures specifically through the Rapid Access Upper GI Cancer Service **(Table 5.3)** and for those who had their gastroscopies through any other elective routes **(Table 5.4)**.

Table 5.2 The total number of local individuals undergoing elective (non-emergency) Gastroscopy across the local GP practice tertile groups and their spectrum of indications (symptoms) and diagnosis profiles.

	Total	**Low**	**Middle**	**High**	**p value**
Number of practices, **n**	63	21	21	21	n/s
Age-sex adjusted gastroscopy rate, **Mean (SD)**	11.5 (4.1)	7.3 (1.2)	11.0 (0.98)	16.3 (2.7)	<0.0001
Number of patients	13082	2115	3969	6998	<0.001
Age, **Mean (SD)**	56 (17)	59 (16)	57 (17)	55 (17)	<0.001
Over 55 **n,%**	7272 (55.6)	1307 (61.8)	2283 (57.5)	3682 (52.6)	<0.001
Under 55 **n,%**	5810 (44.4)	808 (38.2)	1686 (42.5)	3316 (47.4)	
Gender					
Female **n,%**	7364 (56.3)	1181 (55.8)	2195 (55.3)	3988 (57.0)	n/s
Male **n,%**	5718 (43.7)	934 (44.2)	1774 (44.7)	3010 (43.0)	
Symptoms profile					
Alarm symptoms **n,%**	6266 (47.9)	1064 (50.3)	1936 (48.8)	3266 (46.7)	0.006
Non-Alarm **n,%**	6816 (52.1)	1051 (49.7)	2033 (51.2)	3732 (53.3)	
Diagnosis profile					
OG cancer **n,%**	182 (1.4)	46 (2.2)	64 (1.6)	72 (1.0)	<0.001
Serious Benign **n,%**	3907 (29.9)	662 (31.3)	1221 (30.8)	2024 (28.9)	0.037
Normal or Mild **n,%**	8993 (68.7)	1407 (66.5)	2684 (67.6)	4902 (70.0)	0.002

Table 5.3 The number of local individuals had their elective Gastroscopy through RAUGICS system across the local GP practice tertile groups and their spectrum of indications (symptoms) and diagnosis profiles.

	Total	**Low**	**Middle**	**High**	**p value**
Number of patients	4003	549	1048	2406	
Age, **Mean (SD)**	60(16)	64(15)	61(16)	59(16)	<0.001
Over 55 **n,%**	2630 (65.7)	415 (75.6)	714 (68.1)	1501 (62.4)	<0.001
Under 55 **n,%**	1373 (34.3)	134 (24.4)	334 (31.9)	905 (37.6)	
Gender					
Female **n,%**	2332 (58.3)	313 (57.0)	584 (55.7)	1435 (59.6)	n/s
Male **n,%**	1671 (41.7)	236 (43.0)	464 (44.3)	971 (40.4)	
Symptoms profile					
Alarm symptoms **n,%**	3062 (76.5)	413 (75.2)	816 (77.9)	1833 (76.2)	n/s
Non-Alarm **n,%**	941 (23.5)	136 (24.8)	232 (22.1)	573 (23.8)	
Diagnosis profile					
OG cancer **n,%**	95 (2.4)	26 (4.7)	29 (2.8)	40 (1.7)	<0.001
Serious Benign **n,%**	1182 (29.5)	163 (29.7)	326 (31.1)	693 (28.8)	n/s
Normal or Mild **n,%**	2726 (68.1)	360 (65.6)	693 (66.1)	1673 (69.5)	0.056

Table 5.4 The number of local individuals who had their gastroscopy through non-RAUGICS elective pathways and their spectrum of indications (symptoms) and diagnosis profiles across the local GP practice tertile groups.

	Total	**Low**	**Middle**	**High**	**p value**
Number of patients	9079	1566	2921	4592	
Age, **Mean (SD)**	57 (17)	57 (17)	56 (17)	53 (17)	<0.001
Over 55 **n,%**	892 (57.0)	892 (57.0)	1569 (53.7)	2181 (47.5)	<0.001
Under 55 **n,%**	674 (43.0)	674 (43.0)	1352 (46.3)	2411 (52.5)	
Gender					
Female **n,%**	5032 (55.4)	868 (55.4)	1611 (55.2)	2553 (55.6)	n/s
Male **n,%**	4047 (44.6)	698 (44.6)	1310 (44.8)	2039 (44.4)	
Symptoms profile					
Alarm symptoms **n,%**	3204 (35.3)	651 (41.6)	1120 (38.3)	1433 (31.2)	<0.001
Non-Alarm **n,%**	5875 (64.7)	915 (58.4)	1801 (61.7)	3159 (68.8)	
Diagnosis profile					
OG cancer **n,%**	87 (1.0)	20 (1.3)	35 (1.2)	32 (0.7)	0.03
Serious Benign **n,%**	2725 (30.0)	499 (31.9)	895 (30.6)	1331 (29.0)	n/s
Normal or Mild **n,%**	6267 (69.0)	1047 (66.9)	1991 (68.2)	3229 (70.3)	0.01

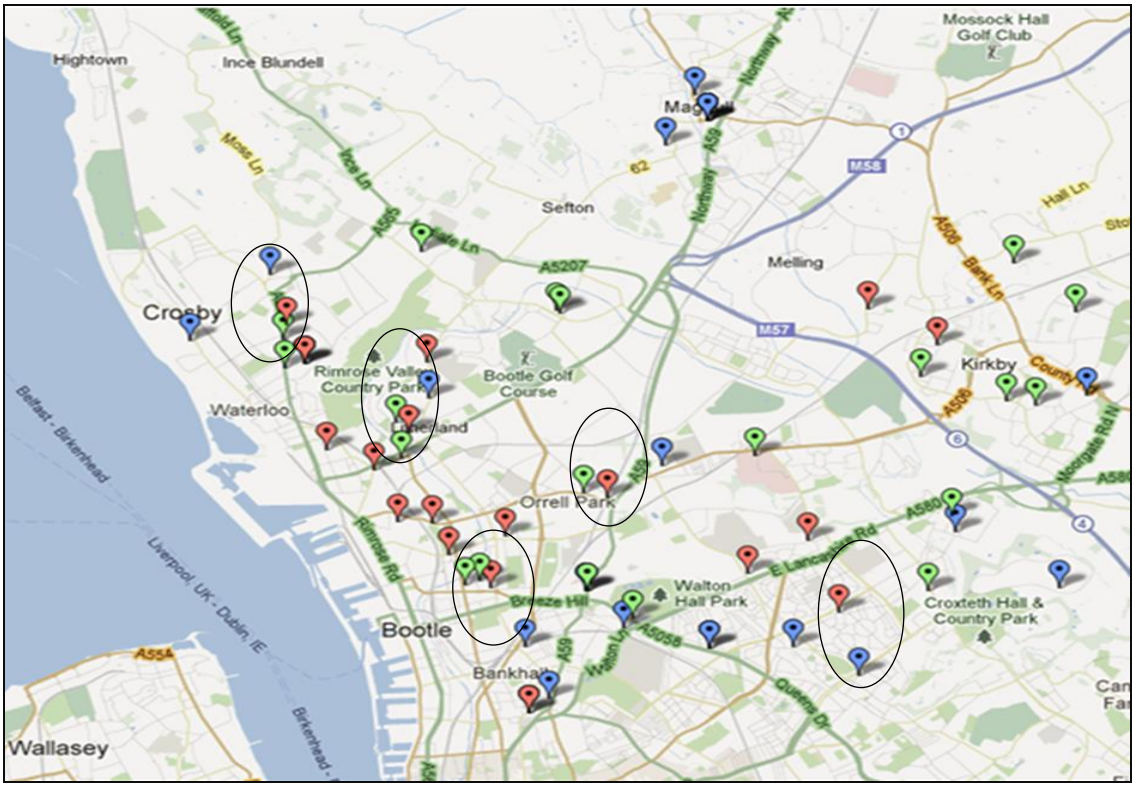
5.4.3 Small area variation in gastroscopy rate across general practices

5.4.3.1 National Intra-PCT variation

Of the 152 PCTs in England, variation across the range of gastroscopy rates among practices in each PCT was less than fivefold in 10 PCTs (6.6%), 5–10-fold in 49 PCTs (32.2%), and more than 10-fold in the remaining 94 PCTs (61.4%). This demonstrates that practices in relatively close proximity to one another, and served by the same local group of hospitals, show a wide spectrum of per capita gastroscopy rates. This would support the role of general practitioner referral policies as a key determinant of gastroscopy rate, rather than simply the local burden of disease.

5.4.3.2 Local geographical mapping of general practices

Geographical mapping of practices in our local area according to gastroscopy rate has shown low, middle and high gastroscopy referring practices within small distances of each other (e.g. 2 miles). This confirms very wide inter-practice variation in gastroscopy rate among practices served by the same local endoscopy services **(Figure 5.6)**.



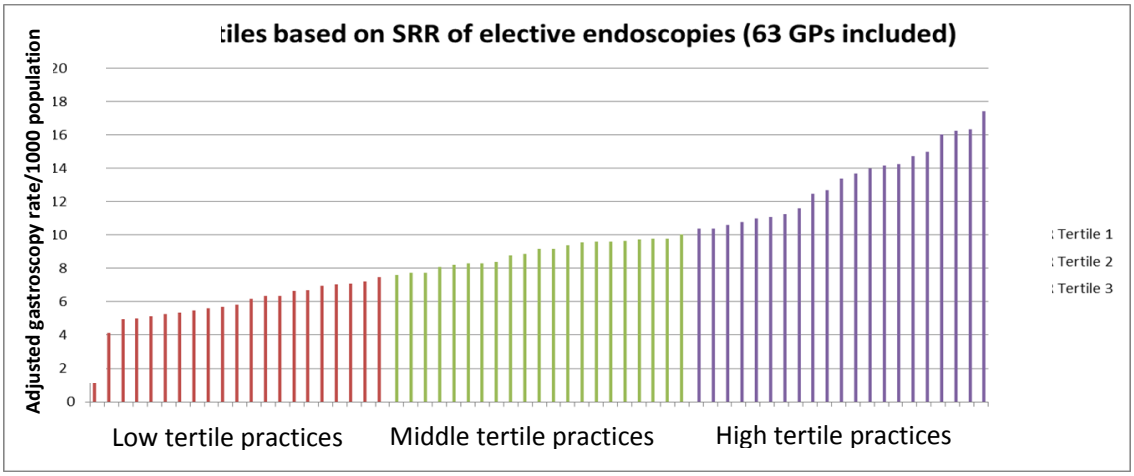


Figure 5.6 Presents mapping of local practices according to their distribution of gastroscopy rate. Google Fusion Table [322]

5.4.4 The association between practice per capita rates of elective gastroscopy and the rate of two week wait referrals for any form of cancer

For practices in the national study, comparison across the elective gastroscopy rate tertiles show small but significant variation in rates of fast-track (TWW) referrals for suspected cancer. The mean rate of TWW referral for any form of cancer was lowest for the low gastroscopy rate tertile and highest for the group of practices in the high tertile **(Figure 5.7)**.

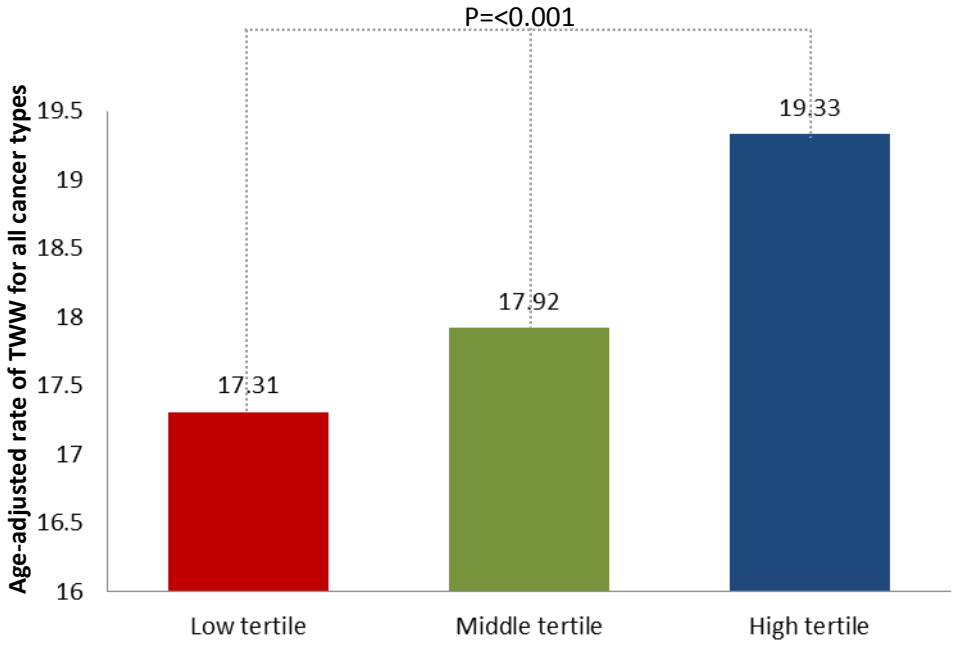
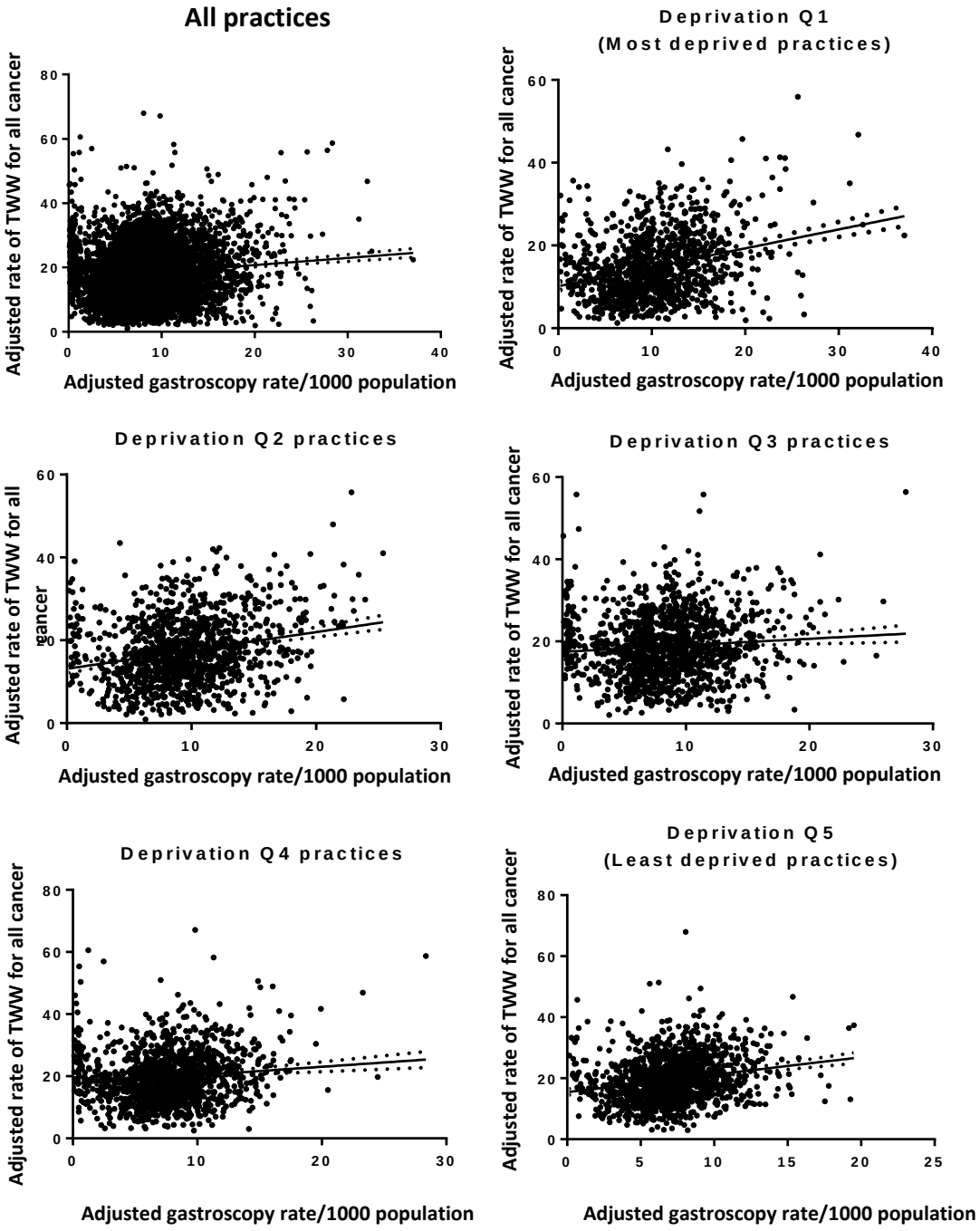


Figure 5.7 Mean rates of two week wait referrals for any form of cancer across the national tertiles of general practice gastroscopy rates (low, middle or high)

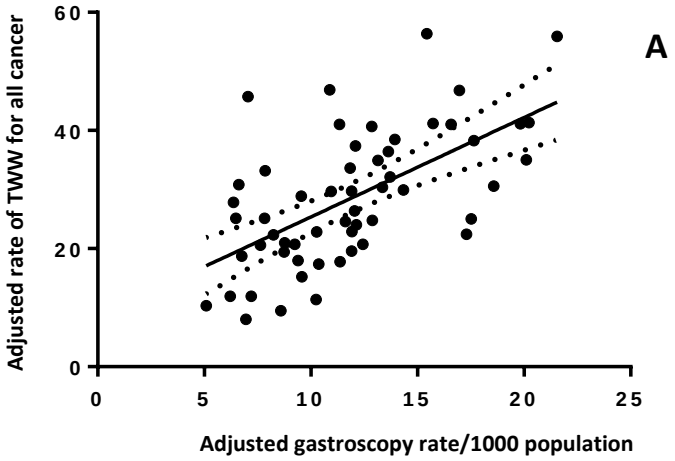
Nationally, the practice gastroscopy rates and the general rate of TWW referrals show **modest** but **consistently** positive correlations overall and across the deprivation quintiles **(Figure 5.8)**. This suggests at practice level there are shared factors that determine the two rates of referral that are not related to age profile of the population (as the rates are age-adjusted), nor specific to deprived or affluent areas.

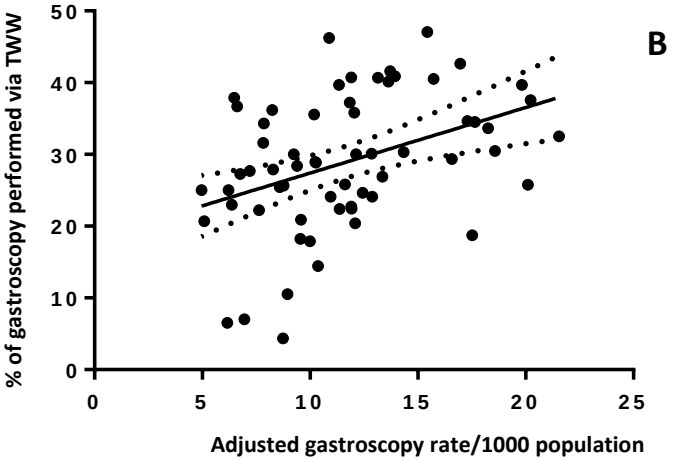
Locally, the strength of the association between the two rates was stronger. Clearly, the local study excludes or reduces the influence of local symptom or disease prevalence, consultation behaviour or variable access to local secondary care diagnostics. **Figure 5.9** shows stronger correlation with higher R squared values. The simple message appears to be that practices that are ‘low’ for gastroscopy also tend to be ‘low’ for TWW referrals in general. This could be consistent with varying 'thresholds' for referral operating among groups of doctors in practices. There are unlikely to be differing burdens of symptoms or cancer incidence across a relatively small geographical area and the mapping exercise confirmed that high and low tertile practices can be located within 1-2 miles.



	Pearson r	95% CI	R^2 Squared	P value
All practices	0.112	0.087-0.136	0.012	<0.001
Q1	0.289	0.233-0.342	0.083	<0.001
Q2	0.231	0.177-0.283	0.053	<0.001
Q3	0.083	0.029-0.136	0.007	0.0026
Q4	0.119	0.066-0.171	0.014	<0.001
Q5	0.211	0.16-0.26	0.045	<0.001

Figure 5.8 Shows the association between the primary care rate of gastroscopy and the rate of two week wait referral for all cancer in general and across practice deprivation quintile.





	Pearson r	95% CI	R^2 Squared	P value
A	0.604	0.405-0.748	0.365	<0.001
B	0.398	0.164-0.589	0.158	0.001

Figure 5.9 Shows the local level association between the primary care rate of gastroscopy and **(A)** the rate of two week wait referral for all cancer in general, and with **(B)** The percentage of gastroscopy performed though TWW system.

5.5 Discussion

This study demonstrates that practices with low rates of gastroscopy tend to have higher "diagnostic yield" of serious pathology. Although a higher yield may be regarded as more consistent with closer adherence to referral guidelines, it may also reflect a more restrictive "gatekeeper" approach or even indicate an increased risk of delayed referral i.e. at a later stage in the disease process. The trends in both the national and local results strongly support this finding, particularly with the presence of a higher mean age at endoscopy among low referring practices. This data could also suggest that high referring practices are more likely to refer patients with low risk "but not no risk" symptoms.

This chapter further explores the extent of these variations within each Primary Care Trust, indicating that in over 90% of PCTs in England there is evidence for over two-fold variation in gastroscopy rates across the local practices and a fifth of the PCTs exhibited more than 5-fold local variation. This, along with the mapping results of local practices according to their tertile, demonstrates that practices in very close proximity to one another and serviced by the same endoscopy unit still often show different referrer rates. This would support the contention that the role of general practitioner referral policies is a significant determinant of gastroscopy rate, rather than just factors such as the local burden of disease or access to local hospital services or data issues (e.g. variable hospital coding).

There is a weak but consistently positive correlation at the practice level between gastroscopy rates and referral rates for suspected cancer in general under the two week wait route. This association is stronger (higher R squared values) at the local level than nationally, perhaps reflecting the exclusion or reduction of confounding influences of local symptom or disease prevalence, consultation behaviour or variable access to local secondary care diagnostics; factors which would be hard to control for at the national level. It is reasonable to suggest that variation in referral behaviour explains the observed association between age-adjusted referral rates for the two week wait system in general (all cancers) and rates of gastroscopy. Meechan et al, also shows that referral rates per capita for TWW are directly correlated to the proportion of cancers treated actively that were 2WW referrals ("detection rate") – i.e. high referral rates into the fast-track system are associated with a great proportion of cancer cases being treated actively.[324] Furthermore, they show that referral rates per capita for TWW are inversely related to the proportion of 2WW referrals which result in a cancer diagnosis ("conversion rate") – i.e. high referral rates into the fast-track system are associated with a lower yield of pathology.[324] Although a low conversion rate might imply inefficient use of the 2WW referral system, the higher the detection rate (active treatment) could reflect better patients outcomes with fewer patients diagnosed via other routes.[122] While the referral rate could give us a general view on the behaviour of the referral practice which is the aim of this part of the study, the relation between detection rate and conversion rate appears to be more informative in term of the appropriateness of clinical practice.[324] However, our data show that

whilst high levels of gastroscopy referral are associated with a low yield of serious pathology (i.e. a "low conversion rate" for gastroscopy in general), such high referral rates are also linked to better OG outcomes such as surgical resection (i.e. a "high" detection rate).

We acknowledge the role of individual patients' care-seeking behaviour as a factor in determining consultation, and hence, gastroscopy referral. However, it is unlikely that such individual factors could operate within one general practice population, and yet not operate within neighbouring populations, and still produce the magnitude of variation we have observed.

However, it must be acknowledged that there is potential for variation in rates of investigation as a result of differences in disease burden and/or health care seeking behaviour and that these population factors may be influenced by deprivation status. [325, 326]

*" **Evidence has been reported of variation by deprivation status in the use of primary care services and in hospital admission patterns. The fourth national study of morbidity statistics from general practice found that patients from deprived areas were more likely to consult a general practitioner with a complaint subsequently diagnosed as cancer** " [77]*

However, evidence was presented in chapter 4 to show that deprivation explains less than 8% of the observed variation in age- and sex-adjusted gastroscopy rates across England. There is no simple association between the multiple underlying causes of dyspepsia and socio-economic status. The local studies presented in this

chapter replicate the trends observed in national data. Our centre serves a relatively homogenous, predominantly urban population in which major cultural differences in consultation behaviour or disease burden are unlikely factors in explaining small area variation in gastroscopy rates.

Local findings are in support of our argument that low gastroscopy referring practices are likely to include a greater proportion of practitioners with a more restrictive "gatekeeper" approach. This is supported by local results (Tables 5.2, 5.3, and 5.4) which demonstrate that these group of practices are reserving gastroscopy for older patients (significantly higher percentage of those over 55 years); to those with more severe symptoms (significantly higher percentages of individuals presented with alarm symptoms). The proportion of patients with serious disease also increased in the same pattern, with low tertile practices having the highest proportion of serious disease (i.e. OG cancers).

Recent evidence results from the analysis of data from the 2010 National Cancer Patient Experience Survey in England suggests that 'primary care' delay is an important factor in OG cancer, in which between 25% of oesophageal and 36% of gastric cancer cases had three or more consultations with their GP before referral.[326] The first National Audit of Cancer Diagnosis in Primary Care also shows that only 50% were referred through urgent (fast-track) pathways.[182] Another qualitative study using data from this national audit, involving the analysis of free text, comments on possible causes for avoidable delays in diagnosis. It notes that, according to the perceptions of participating GPs, the commonest reasons for

delay for oesophageal and gastric cancer patients were GP assessments (16%, 14% respectively), referral delays (32%, 23% respectively) and investigation delays (27%, 34% respectively).[327]

Previous experience from Scotland also showed that around 25% of patients diagnosed with upper GI cancer were not referred for a month or more following their first GP presentation.[318] The same group also showed that oesophago-gastric cancer was among the cancer types with the lowest 'pick up' rate of referrals with an eventual diagnosis of cancer (11.2%) and that around 2% of those whose referral did not meet the urgent suspected cancer criteria did in fact have a diagnosis of cancer. [318]

A recent study by Hansen et al (2011) also highlights the possible association between delayed cancer diagnosis and GP practice characteristics. [167] however, variables such as GP gender, age, CME activity, and practice list size are identified as explaining only a tiny part of the variation.[167]

Thus, it remains an open question whether some of the variation in gastroscopy rate, as well as cancer outcome, can be explained by other factors relating to the interaction between patients and GP practice characteristics. Our study shows that lower threshold for referring with lower risk symptoms were among the high referring practices. This could also suggest that GP doctors' professional and individual interpretations of NICE guidance in dyspepsia management may influence both their communication about patients' symptoms, and also the timing of their referrals for gastroscopy. It is important to note that this does not imply that there is either a lack of knowledge or poor medical performance, but it could

mainly reflect diagnostic features, their sensitivity of the appraisal of cancer symptoms and their attitudes towards risk.

It is well recognised that clinical history is a poor guide to the underlying diagnosis of dyspepsia. [328] Hence, a better way of detecting symptomatic patients as they present to their general practitioner is required [91, 329], in addition to a more advanced system for validating referral guidelines intended to reduce the number of inappropriate referrals within the system. Of further concern is the fact that data from other interventional studies remains limited. Although such data might support or refute our findings, policies that actively encourage restriction of gastroscopy procedures to investigate dyspepsia may have unintended adverse impacts on long term survival from OG cancer.

The national diagnostic profile analysis shows that upper gastrointestinal malignancy accounted for only 2.1% of all patients undergoing gastroscopy investigation. This represents OG cancer cases coded for those who had all gastroscopy procedures performed through various elective routes, including the two week wait system. It is one of the HES related limitations that it cannot be possible to distinguish between patients who started their journey through various elective routes.

It is worth mentioning that the local audit finding for gastroscopy diagnosis profile not only acts in support of the study hypothesis but also shows the potential of using HES data despite the known issues of its coding – our algorithms used to interrogate HES data produced very similar findings in national data as those found in local data that relied on original gastroscopy reports. Hence, the local audit work

adds further validation steps to the methods used for selection of the most likely codes for the described national diagnostic categories.

It is difficult to define what would be the "ideal" rate of gastroscopy at the level of GP practices, nor is it possible to identify whether 'low' or 'high' rates are inappropriate at an individual practice. Arguably, low rates of negative investigation and a high diagnostic yield are desirable but not if the positive diagnosis occurs at a late, incurable stage. In the case of OG cancer, if earlier diagnosis is to be achieved then more evidence is needed to support primary care and less restrictive guidelines would be required to allow adoption of lower threshold for referring individuals with lower risk symptoms ('low risk, but not no risk'). The overall message of guidelines for dyspepsia supports a "watch and wait approach" and managerial and financial focus is on high rates and perceived "over-referral". Nevertheless, the data techniques developed and tested in this work show potential for exploring small area variation and focussing not only on 'high' referrers. It is possible to identify practice populations with particularly low rates of investigation compared to adjacent practices. Local cancer initiatives could explore the reasons why a minority of local practice populations have unexpectedly low referral rates compared with local norms.

Chapter 6: General discussion and future directions

6.1 Overall summary of the thesis

This thesis has sought to explore national inequalities in outcome for oesophago-gastric cancer in England, and whether such disparity is associated with the variation in gastroscopy rates in General Practice populations. This section is intended to summarize the main purpose of each chapter as well as pointing out the key achievements and contributions of the research, with reference to the three main aims and objectives listed in **(Chapter 2)**.

In brief, the first chapter **(Chapter 1)** provides a general clinical overview of OG cancer and describes service provision and organization of care in England. It highlights the challenging 'gate-keeper' role played by general practitioners in distinguishing the large majority of dyspeptic patients who have functional or benign underlying causes (who can be managed effectively within the primary care setting without invasive investigation) from those with sinister disease who need referral for specialist diagnostic investigation. The process of making this distinction is complicated by unresolved controversy regarding the optimum role of gastroscopy in managing dyspepsia and the imperfect evidence-base for existing referral guidelines. The chapter then summarizes the literature regarding variations in health care and the ways that health care systems make use of clinical indicators to study inequality or unwarranted variation. The chapter further aims to familiarize the reader with the nature of routinely collected health care information, with particular attention on Hospital Episode Statistics (HES) – considering both its potential weaknesses (relating to data quality and the relatively limited clinical content) and it's growing application in developing measures aimed at driving improved care and outcomes.

Chapter 2 presented the rationale for the study, with a direct exploration of the gap in knowledge as identified from the literature review. This review had helped establish the original hypothesis and aims of the study. Additionally, this central part of the thesis along with the supporting appendices **(Chapter 7)** details our innovative method of developing a more clinically directed approach in using HES data to identify OG cancer patients population with pathways of care compatible with new incident cases. The successful validation of this complex linkage method as presented in **(Chapter 3)** was a key research milestone in the course of the project.

Chapter 3 provides the first results, assessing the reliability of our database inclusions, coding algorithms and linkage methodology, and testing the face validity using both national and local (Audit) data output. In addition, the same chapter describes the association between cancer outcomes and some patient level variables, such as age, sex, co-morbidity and deprivation status.

Chapter 4 confirms the wide variability in per capita rates of gastroscopy at the level of general practice populations, which cannot be explained by patients' demographics. It also reports the novel finding that variation in rates of gastroscopy at the level of general practice populations is associated with outcome of oesophageal and gastric cancers.[315] More specifically, GP gastroscopy rates act as a predictor of cancer outcome, after adjusting for various confounders. [315]

The final study of the thesis, described in **(Chapter 5)**, confirms that practices with relatively low rates of gastrosopy (low tertile) are shown to be operating more selective referral practices with a stronger gatekeeper approach, thereby reserving

gastroscopy for older patients or for those with more severe symptoms (e.g. alarm symptoms) associated with serious disease. On the other hand, practitioners at high tertile practices tend to have a lower threshold for gastroscopy referral, most of which produce a normal gastroscopy finding. This is suggestive of the fact that high gastroscopy practices are presumably investigating more non-NICE symptom patients.

The factors responsible for difference in gastroscopy rate between general practices populations are likely to be complex, including differences in local symptom prevalence and 'care seeking behaviour' and possible differences in GP access to hospital-based gastroscopy services.[114] However, the finding of wide variation within relatively small geographical areas suggests a role for unexplained variation.[314]

In other words, the magnitude of this variation is still difficult to be explained by these local factors alone. This claim is supported by, first, local mapping which shows that such variation is apparent between practices within a very close geographical distance to each other, serviced by the same hospital or Endoscopy Unit. Secondly, our national linkage to the NCIN two week wait referral rate for all cancer data shows that low tertile practices are not only low for referring for gastroscopy but are also low in using the two week wait referral system (and yet according to the national cancer plan, this pathway should be unrestricted for most suspected cancer patients).

Although it is difficult to measure individual patients' consultation behaviour, which it is expected might influence results, our analysis of using only practices within the most socially disadvantaged group whose population, according to the published literature, tend to have higher consultation rate showed a relatively stronger association.

Although the approach of the practices within the low tertile group can be seen as more consistent with the current guidelines policies at one end, it has also been suggested that these guidelines could discourage some GPs from using what has been described as their "sixth sense" in deciding which patients need to be referred.[319]

The two week wait pick-up rates reported in various studies suggest that this pathway is still diagnosing a low proportion of patients with OG cancer. [302, 330] Our local endoscopy audit shows that 2.4 % of patients going via RAUGICS were diagnosed with OG cancer, with a local tertile diagnostic yielding a range from 4.7 % in high referring practices to 1.7% among low tertile practices. Whilst such fast tracking does increase the overall yield of diagnosis of cancer in all tertiles (Low, Middle and High), the yield remains relatively small, given the considerable workload required.

Having shown that low tertile group of practices tend to produce the worst cancer outcomes, particularly in the most deprived areas in the country, we strongly recommend that the current guidelines are re-evaluated, providing clearer criteria for identifying the best candidates to have gastroscopy at the right time. It is hoped that the findings of this study will at least encourage further debate in this area.

6.2 Methodological challenges, strengths, weaknesses and limitations

The reporting of the epidemiological research in this thesis follows STROBE guidelines (Strengthening the reporting of observational studies in epidemiology) to provide the essential information on methodology and findings. [331]

The strengths of our study include the novel application of clinically-developed algorithms to analyse the chronological sequence of coded care episodes for each patient, our verification of the techniques by direct comparison to a local patient-level audit, and the validation of the patient population and outcome variables against independent external sources of national data for OG cancer. Hence, this was not simply a top-down analysis of HES data, but rather took several validation steps to confirm the methodology, minimise the risk of data errors and to check the clinical face-validity of the outputs.

Extensive use of sensitivity analyses was undertaken with respect to the 'exposure' variable of interest (rate of gastroscopy in the general practice population), starting with aggregation into tertiles of age- and sex-adjusted rate but re-testing the associations using quintiles and absolute (continuous) rates including the gastroscopy rate for people over the age of 55 years.

A benefit of using this logistic regression method is that it permits adjustment both by categorical variables and by continuous variables.[332] Hence, we have further confirmed the study findings, even after substituting the practice level categorical variable (aggregations of practices into tertile or quintile groups) for a continuous scale variable, reflecting the actual rate of gastroscopy at each individual practice.

Weaknesses and limitations of the research relate to the generic concern regarding the completeness, precision and depth of routine administrative coding. We applied transparent inclusion/exclusion criteria and validation steps to limit the impact of coding error, and tested our hypothesis against three outcome variables.

A separate analysis of different sub-groups of OG cancers based on anatomical location or histology was not possible within routine coding, but this was not relevant to the primary study question. Although a small number of patients are diagnosed or referred from the private sector, the data for this minority of patients are not easily available. [277]

Lack of the clinical information provided by GPs as well as staging of the disease within HES are considered as another limitations, which have prevented this study from measuring the benefit of gastroscopy rate in identifying early stage disease at the national level. This study was also limited by not having information on patient behaviour, exercise, diet, smoking and drinking habit. [268, 333] These factors are thought to be partly or largely beyond the GPs' control, and they might also influence poorer cancer outcomes.[333]

In addition, GP practice level information is limited particularly at the national level, and the associations between QOF scores and various outcomes such as emergency admissions and mortality were described as small and inconsistent.[292] The influence of deprivation status on the outcomes was considerably stronger.[334]

The focus of this thesis is on the potential for primary care delay in the diagnosis of OG cancers, and specifically on the key decision to refer for elective gastroscopy

with the provision of current guidelines. The outcome variables were selected in this research to reflect the diagnostic pathway, rather than subsequent hospital-based care or treatment outcome. As illustrated by our intra PCT variation, local gastroscopy audit data and geographical mapping, we find that practices within the same geographical area are distributed across different tertiles and yet are served by the same hospitals. In other words, an individual hospital will serve practices across a spectrum of referral rates. Hence, we do not believe that institutional variation is relevant to our primary analysis.

Both "first ever" gastroscopies and "re-referrals" would be captured within total elective activity counts aggregated at general practice level. These are both relevant to exploring GP thresholds for referral and re-referral when dealing with dyspeptic patients. It is true that a proportion of repeat procedures will be follow-up 'scopes initiated by hospitals (e.g. gastric ulcer healing) and a very small contribution from elective screening programmes (e.g. re-calls by hospitals for Barrett's "*surveillance*") but the vast majority of elective gastroscopy activity is for symptomatic dyspeptic patients. Within the study period, the majority (88.2%) of the procedures were coded for the "first-time" for the included patients within the 2-year time window. Most importantly, comparable figures were observed between practice tertiles. It would be hard to consider that some putative hospital-based factor related to differing local policies for repeat scopes or Barrett's surveillance could lead to a systematic bias in this study – the variation of interest is reasonably between general practices exhibiting wide variation in rates of investigation. Furthermore, only a tiny minority of total oesophageal adenocarcinoma cases are

diagnosed within Barrett's surveillance programmes [335] and unlikely to be of relevance to our study of OG cancer and GP-level variation. When analysing diagnostic profiles of investigated patients across the three groups of practices, we show a very clear gradient both in average age and rate of "major pathologies" from low, through middle to high tertile practices. This is consistent with the grouping of practices being a valid surrogate marker for differing thresholds of referral for gastroscopy.

Delay in seeking medical care after symptom onset is a potential factor in delayed cancer diagnosis.[33, 181] This relates partially to the biological nature and anatomical location of these tumours—a factor common to all patients, and hence not a confounding influence as such in this study.

A range of socioeconomic characteristics has been associated with consultation behaviour in primary care which might reflect "patient delay" [336], but our analysis adjusts for age, gender and socioeconomic status. We acknowledge a role for patient behavioural factors in determining consultation, and hence gastroscopy referral. However, it is unlikely that such individual factors could operate systematically within one general practice population, and not within neighbouring populations, and yet still create the magnitude of variation we have observed within individual PCTs and in our locality. Therefore, further research is required to better understand the causes for practice-level variation in gastroscopy rates.

6.3 Clinical and research implications and future direction.

The finding of this study could be used to inform both national guidance and local initiatives aimed at improving outcomes for OG cancer through earlier diagnosis. This study suggests that practices with low rates of gastroscopy should review their practice. It has been highlighted that the inequality in outcome with respect to gastroscopy rate was greater in magnitude when practices were grouped according to gastroscopy in >55 year olds. This implies that new guidelines should consider a lower threshold for referral in older subjects, rather than the current emphasis on alarm symptoms. Furthermore, there is scope for targeted local initiatives to ensure appropriate rates of gastroscopy in practices serving socioeconomically disadvantaged areas.

There is a legitimate focus on identifying and constraining "unnecessary" use of expensive secondary care investigations specially in the present climate of cost containment in the UK healthcare system. However, this study has revealed that practices with the lowest rates of gastroscopy tend to achieve the worst outcomes for OG cancer, particularly in those living in the most deprived areas. Local initiatives aimed at reducing gastroscopy activity may well avoid excessive investigations for younger patients with benign condition without affecting clinical outcome. However, this study suggests that there is a need to concentrate on both ends of the referral spectrum.[315]

Our findings should stimulate research to establish the costs and benefits of programmes designed to encourage targeted increases in gastroscopy rates in selected local populations. If the situation is to improve, revision of current referral

guidelines requires urgent attention, along with strategies for managing patients with low risk symptoms and to support compliance.[315]

More than 13.6 million people are served by low tertile practices. If this population experienced similar average gastroscopy rate as the middle tertile group (8.1 per 1,000), we estimate that this would require 49,301 extra procedures. Assuming a daycase gastroscopy cost of £431 [337] this would cost £21,325,250 nationally. If this increase in gastroscopy activity results in the same surgical resection rate as shown by the middle tertile group, this implies a 0.95% absolute rise (15.44% to 16.39%) or an extra 59 surgical candidates from low tertile practices (0.95% of 6,196 patients). This suggests a cost of over £360,000 per additional potential surgical cure.[315]

Published median survival for un-resectable OG cancers are approximately 6-9 months [338] whereas corresponding survival data reported after radical surgery are 27-38 months.[339, 340] Thus, it has been estimated that diagnosis at an operable stage may extend life by 18-32 months on average (around 2.5 years). This puts the crude cost-per-life-year saved for our hypothetical scenario at around £140,000. Alternatively, it is known that only about a fifth of surgical cases achieve 5-year survival and potential long term cure [177] – this equates to just 12 lives saved of the 59 predicted extra surgical cases at a cost of £21.3 Million.[315]

This crude calculation relies on simplistic assumptions, and a formal economic analysis would be required to model the full stream of potential costs and benefits arising from interventions to modify gastroscopy referral practice.[315]

Nevertheless, our estimate suggests that a simple strategy to encourage a generalized increase in gastroscopy across all populations served by the 'low tertile' practices appears costly compared to alternative healthcare investments. Scarce resources might be deployed more cost-effectively within gastroenterology by increasing rates of other tests such as colonoscopy. Economic models exploring the cost-effectiveness of a range of colonoscopy-based screening strategies for colorectal cancer have suggested a cost per life-year saved below a threshold of US$ 40,000 (£25,000). [315, 341]

In practice, a range of alternative strategies might address current inequalities in OG cancer outcome but at lower opportunity costs. We favour more targeted locally-led intervention to enable general practitioners to identify whether their gastroscopy rates are low in relation to local norms (i.e. "local outliers"), particularly in socioeconomically disadvantaged areas, with a focus on increasing access to gastroscopy for older subjects at risk of cancer. Costs could be offset by simultaneous efforts to encourage reductions in gastroscopy among younger dyspeptic patients where non-invasive strategies are appropriate [147], targeting practices at the high end of the referral volume continuum. The local generation and sharing of practice-level comparative data on gastroscopy could allow GPs, commissioners and endoscopy units to work together to reduce inequalities.

One of the reasons for delay in OG cancer diagnosis could be that patients have poor understanding or awareness of its main signs and symptoms.[342-344] A previous study shows that around two thirds of cases were symptomatic for more than 3 months. [345] Local study in Liverpool included 37,500 individuals over 40

years of age who were registered with 12 general practices tests the efficacy of education by home letter, found that this intervention produce improvement in resection rate and curability, but the longer term survival was not affected.[346] Although improving the survival of OG cancer is likely to require more complex and intensive interventions, still a new public health campaigns for the awareness of symptoms and risk factors at the national level are important if the cancer is to be detected at an earlier and potentially curable stage.[347] Such argument could be supported by the recent media campaigns in England which planned to increase awareness of symptoms of colon cancer, have improved public alertness of its common symptoms. This was accompanied with a concurrent increase of about 50% in patients attending their GP with symptoms of change in bowel habit and/or rectal bleeding, along with comparable increases in urgent referrals and colonoscopy.[348] Finding of our research could therefore be used to better direct similar intervention specially among the most disadvantaged members of the society whom particularly belong to low referring practices.

The magnitude of variation we have shown in rates of gastroscopy is consistent with wide differences in clinical practice across primary care and possible inequalities in access to investigation. Although national NICE guidelines were originally expected to reduce such variation, for some cancer types, tools such as the Risk Assessment Tool (RATs) [349] and “Qcancer” [329, 350] (both of which might act to improve case selection) could be the way forward in helping GPs to better judge the individual patient’s likelihood of cancer and to select those who have symptoms of potential cancer, but who do not qualify under the NICE

guidance for specialist referral and/or further investigation. These tools are based on the epidemiology of cancer symptoms in primary care by giving risk estimates for patients presenting with for example, single symptom of cancer, pairs of symptoms and repeat attendances.[351]

For example, the National Cancer Action Team publication,[349] which evaluates the utilization of RATs for suspected cancer in general practice, showed that patients with higher risk scores were more likely to be investigated. The qualitative part of the same study illustrates that RATs raised the GPs' willingness to investigate for cancer and it also helped provide reassurance when investigation was not needed, especially in patients with atypical presentations.[349]

Even though these tools appear logical and might offer the potential for the improved use of the available resources, more research will still be required to overcome the challenge of how best to incorporate these risk tools into routine clinical practice.[351]

It is also expected that these risk modules might not be applicable in the cases of suspected OG cancers without a corresponding reduction in the unit cost of providing endoscopy, so that individuals with low risk (but not no risk) dyspepsia symptoms can be offered prompt endoscopy.

However, a better understanding how cancer outcome relates to previous encounters with primary care is essential. Therefore, further research efforts encompassing both HES and more detailed primary care records will be crucial to

help examine how existing information and databases can be better used to improve cancer outcomes.

6.4 Conclusion and recommendations

In the context of health service research, the results of this study support the idea that HES data can be especially powerful when carefully interpreted with clinical background knowledge, and that it has an unexplored potential for producing answers to clinical research questions. The national-level analysis provides 'real-world' descriptive statistics for OG cancer care in England, which has been adequately validated against recently published clinical audits and other statistics to eliminate the worry of selection bias.

There remain inequalities in outcome for oesophago-gastric cancer in England and this is associated with gastroscopy rates in general practice populations. There is potential for primary care delay in the diagnosis of OG cancers, and specifically the key decision to refer low risk (but not no risk) patients for elective gastroscopy with the provision of current guideline and route of diagnosis.

Guidelines are proposed to *reduce* variation in practice. However, the association between variation in investigation rates and cancer outcome shown by this study has identified a strong reason to reflect on whether current guidelines are "*fit-for-purpose*" or "*implemented effectively"*. Therefore, this study recommends that practices with low rates of gastroscopy should review their current policies, particularly those serving the most deprived members of the society.

Chapter 7: Appendices, syntaxes and published papers

Appendix 7.1 Specialties included in the analysis

CODE	NAME	STATUS
300	GENERAL MEDICINE	MEDICAL
301	GASTROENTEROLOGY	MEDICAL
302	ENDOCRINOLOGY	MEDICAL
303	CLINICAL HAEMATOLOGY	MEDICAL
305	CLINICAL PHARMACOLOGY	MEDICAL
313	CLINICAL IMMUNOLOGY and ALLERGY	MEDICAL
314	REHABILITATION	MEDICAL
315	PALLIATIVE MEDICINE	MEDICAL
320	CARDIOLOGY	MEDICAL
330	DERMATOLOGY	MEDICAL
340	RESPIRATORY MEDICINE (also known as thoracic medicine)	MEDICAL
350	INFECTIOUS DISEASES	MEDICAL
352	TROPICAL MEDICINE	MEDICAL
360	GENITOURINARY MEDICINE	MEDICAL
361	NEPHROLOGY	MEDICAL
370	MEDICAL ONCOLOGY	MEDICAL
400	NEUROLOGY	MEDICAL
410	RHEUMATOLOGY	MEDICAL
430	GERIATRIC MEDICINE	MEDICAL
823	HAEMATOLOGY	MEDICAL
100	GENERAL SURGERY	SURGICAL
101	UROLOGY	SURGICAL
110	TRAUMA & ORTHOPAEDICS	SURGICAL
120	ENT	SURGICAL
130	OPHTHALMOLOGY	SURGICAL
140	ORAL SURGERY	SURGICAL
145	ORAL & MAXILLO FACIAL SURGERY	SURGICAL
150	NEUROSURGERY	SURGICAL
160	PLASTIC SURGERY	SURGICAL
170	CARDIOTHORACIC SURGERY	SURGICAL
180	ACCIDENT & EMERGENCY	SURGICAL
190	ANAESTHETICS	SURGICAL
192	CRITICAL CARE MEDICINE	SURGICAL

Appendix 7.2 Trust included in the analysis

Between the 2 dataset years Hammersmith (**RQN**) and St Mary's (**RJ5**) hospitals had merged to become Imperial (**RYJ**). RQN codes and RJ5 codes were amended to (**RYJ**). It is also important to note that two surgical centres The Cardiothoracic Centre (**RBQ**) and The Royal Marsden (**RPY**) were added to identify OGC cases who had surgical resection.

PROCODE	DESCRIPTION
5QT	ISLE OF WIGHT PCT
RA2	ROYAL SURREY COUNTY HOSPITAL NHS TRUST
RA3	WESTON AREA HEALTH NHS TRUST
RA4	YEOVIL DISTRICT HOSPITAL NHS FOUNDATION TRUST
RA7	UNIVERSITY HOSPITALS OF BRISTOL NHS FOUNDATION TRUST
RA9	SOUTH DEVON HEALTHCARE NHS FOUNDATION TRUST
RAE	BRADFORD TEACHING HOSPITALS NHS FOUNDATION TRUST
RAJ	SOUTHEND UNIVERSITY HOSPITAL NHS FOUNDATION TRUST
RAL	ROYAL FREE HAMPSTEAD NHS TRUST
RAP	NORTH MIDDLESEX UNIVERSITY HOSPITAL NHS TRUST
RAS	THE HILLINGDON HOSPITAL NHS TRUST
RAX	KINGSTON HOSPITAL NHS TRUST
RBA	TAUNTON AND SOMERSET NHS FOUNDATION TRUST
RBD	DORSET COUNTY HOSPITAL NHS FOUNDATION TRUST
RBK	WALSALL HOSPITALS NHS TRUST
RBL	WIRRAL UNIVERSITY TEACHING HOSPITAL NHS FOUNDATION TRUST
RBN	ST HELENS AND KNOWSLEY HOSPITALS NHS TRUST
RBT	MID CHESHIRE HOSPITALS NHS FOUNDATION TRUST
RBZ	NORTHERN DEVON HEALTHCARE NHS TRUST
RC1	BEDFORD HOSPITAL NHS TRUST
RC3	EALING HOSPITAL NHS TRUST
RC9	LUTON AND DUNSTABLE HOSPITAL NHS FOUNDATION TRUST
RCB	YORK HOSPITALS NHS FOUNDATION TRUST
RCC	SCARBOROUGH AND NORTH EAST YORKSHIRE HEALTH CARE NHS TRUST
RCD	HARROGATE AND DISTRICT NHS FOUNDATION TRUST
RCF	AIREDALE NHS TRUST
RCX	THE QUEEN ELIZABETH HOSPITAL KING'S LYNN NHS TRUST
RD1	ROYAL UNITED HOSPITAL BATH NHS TRUST
RD3	POOLE HOSPITAL NHS FOUNDATION TRUST
RD7	HEATHERWOOD AND WEXHAM PARK HOSPITALS NHS FOUNDATION TRUST
RD8	MILTON KEYNES HOSPITAL NHS FOUNDATION TRUST
RDD	BASILDON AND THURROCK UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
RDE	COLCHESTER HOSPITAL UNIVERSITY NHS FOUNDATION TRUST
RDU	FRIMLEY PARK HOSPITAL NHS FOUNDATION TRUST
RDZ	THE ROYAL BOURNEMOUTH AND CHRISTCHURCH HOSPITALS NHS FOUNDATION TRUST
RE9	SOUTH TYNESIDE NHS FOUNDATION TRUST
REF	ROYAL CORNWALL HOSPITALS NHS TRUST
REM	AINTREE UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
RF4	BARKING, HAVERING AND REDBRIDGE HOSPITALS NHS TRUST
RFF	BARNSLEY HOSPITAL NHS FOUNDATION TRUST
RFR	THE ROTHERHAM NHS FOUNDATION TRUST
RFS	CHESTERFIELD ROYAL HOSPITAL NHS FOUNDATION TRUST
RFW	WEST MIDDLESEX UNIVERSITY HOSPITAL NHS TRUST
RG2	QUEEN ELIZABETH HOSPITAL NHS TRUST
RG3	BROMLEY HOSPITALS NHS TRUST
RGC	WHIPPS CROSS UNIVERSITY HOSPITAL NHS TRUST
RGN	PETERBOROUGH AND STAMFORD HOSPITALS NHS FOUNDATION TRUST

RGP	JAMES PAGET UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
RGQ	IPSWICH HOSPITAL NHS TRUST
RGR	WEST SUFFOLK HOSPITALS NHS TRUST
RGT	CAMBRIDGE UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
RGZ	QUEEN MARY'S SIDCUP NHS TRUST
RH8	ROYAL DEVON AND EXETER NHS FOUNDATION TRUST
RHM	SOUTHAMPTON UNIVERSITY HOSPITALS NHS TRUST
RHQ	SHEFFIELD TEACHING HOSPITALS NHS FOUNDATION TRUST
RHU	PORTSMOUTH HOSPITALS NHS TRUST
RHW	ROYAL BERKSHIRE NHS FOUNDATION TRUST
RJ1	GUY'S AND ST THOMAS' NHS FOUNDATION TRUST
RJ2	THE LEWISHAM HOSPITAL NHS TRUST
RJ5	ST MARYS NHS TRUST
RJ6	MAYDAY HEALTHCARE NHS TRUST
RJ7	ST GEORGE'S HEALTHCARE NHS TRUST
RJC	SOUTH WARWICKSHIRE GENERAL HOSPITALS NHS TRUST
RJD	MID STAFFORDSHIRE NHS FOUNDATION TRUST
RJE	UNIVERSITY HOSPITAL OF NORTH STAFFORDSHIRE NHS TRUST
RJF	BURTON HOSPITALS NHS TRUST
RJL	NORTHERN LINCOLNSHIRE AND GOOLE HOSPITALS NHS FOUNDATION TRUST
RJN	EAST CHESHIRE NHS TRUST
RJR	COUNTESS OF CHESTER HOSPITAL NHS FOUNDATION TRUST
RJZ	KING'S COLLEGE HOSPITAL NHS FOUNDATION TRUST
RK5	SHERWOOD FOREST HOSPITALS NHS FOUNDATION TRUST
RK9	PLYMOUTH HOSPITALS NHS TRUST
RKB	UNIVERSITY HOSPITALS COVENTRY AND WARWICKSHIRE NHS TRUST
RKE	THE WHITTINGTON HOSPITAL NHS TRUST
RL4	THE ROYAL WOLVERHAMPTON HOSPITALS NHS TRUST
RLN	CITY HOSPITALS SUNDERLAND NHS FOUNDATION TRUST
RLQ	HEREFORD HOSPITALS NHS TRUST
RLT	GEORGE ELIOT HOSPITAL NHS TRUST
RM1	NORFOLK AND NORWICH UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
RM2	UNIVERSITY HOSPITAL OF SOUTH MANCHESTER NHS FOUNDATION TRUST
RM3	SALFORD ROYAL NHS FOUNDATION TRUST
RM4	TRAFFORD HEALTHCARE NHS TRUST
RMC	BOLTON HOSPITALS NHS TRUST
RMP	TAMESIDE HOSPITAL NHS FOUNDATION TRUST
RN1	WINCHESTER AND EASTLEIGH HEALTHCARE NHS TRUST
RN3	SWINDON AND MARLBOROUGH NHS TRUST
RN5	BASINGSTOKE AND NORTH HAMPSHIRE NHS FOUNDATION TRUST
RN7	DARTFORD AND GRAVESHAM NHS TRUST
RNA	DUDLEY GROUP OF HOSPITALS NHS TRUST
RNH	NEWHAM UNIVERSITY HOSPITAL NHS TRUST
RNJ	BARTS AND THE LONDON NHS TRUST
RNL	NORTH CUMBRIA UNIVERSITY HOSPITALS NHS TRUST
RNQ	KETTERING GENERAL HOSPITAL NHS TRUST
RNS	NORTHAMPTON GENERAL HOSPITAL NHS TRUST
RNZ	SALISBURY NHS FOUNDATION TRUST
RP5	DONCASTER AND BASSETLAW HOSPITALS NHS FOUNDATION TRUST
RPA	MEDWAY NHS FOUNDATION TRUST
RPL	WORTHING AND SOUTHLANDS HOSPITALS NHS TRUST
RPR	ROYAL WEST SUSSEX NHS TRUST
RQ6	ROYAL LIVERPOOL AND BROADGREEN UNIVERSITY HOSPITALS NHS TRUST
RQ8	MID ESSEX HOSPITAL SERVICES NHS TRUST
RQM	CHELSEA AND WESTMINSTER HOSPITAL NHS FOUNDATION TRUST
RQN	HAMMERSMITH NHS TRUST

RQQ	HINCHINGBROOKE HEALTH CARE NHS TRUST
RQW	THE PRINCESS ALEXANDRA HOSPITAL NHS TRUST
RQX	HOMERTON UNIVERSITY HOSPITAL NHS FOUNDATION TRUST
RR1	HEART OF ENGLAND NHS FOUNDATION TRUST
RR7	GATESHEAD HEALTH NHS FOUNDATION TRUST
RR8	LEEDS TEACHING HOSPITALS NHS TRUST
RRF	WRIGHTINGTON, WIGAN AND LEIGH NHS TRUST
RRK	UNIVERSITY HOSPITAL BIRMINGHAM NHS FOUNDATION TRUST
RRV	UNIVERSITY COLLEGE LONDON HOSPITALS NHS FOUNDATION TRUST
RTD	THE NEWCASTLE UPON TYNE HOSPITALS NHS FOUNDATION TRUST
RTE	GLOUCESTERSHIRE HOSPITALS NHS FOUNDATION TRUST
RTF	NORTHUMBRIA HEALTHCARE NHS FOUNDATION TRUST
RTG	DERBY HOSPITALS NHS FOUNDATION TRUST
RTH	OXFORD RADCLIFFE HOSPITALS NHS TRUST
RTK	ASHFORD AND ST PETER'S HOSPITALS NHS TRUST
RTP	SURREY AND SUSSEX HEALTHCARE NHS TRUST
RTR	SOUTH TEES HOSPITALS NHS TRUST
RTX	UNIVERSITY HOSPITALS OF MORECAMBE BAY NHS TRUST
RV8	NORTH WEST LONDON HOSPITALS NHS TRUST
RVJ	NORTH BRISTOL NHS TRUST
RVL	BARNET AND CHASE FARM HOSPITALS NHS TRUST
RVR	EPSOM AND ST HELIER UNIVERSITY HOSPITALS NHS TRUST
RVV	EAST KENT HOSPITALS UNIVERSITY NHS TRUST
RVW	NORTH TEES AND HARTLEPOOL NHS FOUNDATION TRUST
RVY	SOUTHPORT AND ORMSKIRK HOSPITAL NHS TRUST
RW3	CENTRAL MANCHESTER AND MANCHESTER CHILDREN'S UNIVERSITY HOSPITALS NHS TRUST
RW6	PENNINE ACUTE HOSPITALS NHS TRUST
RWA	HULL AND EAST YORKSHIRE HOSPITALS NHS TRUST
RWD	UNITED LINCOLNSHIRE HOSPITALS NHS TRUST
RWE	UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST
RWF	MAIDSTONE AND TUNBRIDGE WELLS NHS TRUST
RWG	WEST HERTFORDSHIRE HOSPITALS NHS TRUST
RWH	EAST AND NORTH HERTFORDSHIRE NHS TRUST
RWJ	STOCKPORT NHS FOUNDATION TRUST
RWP	WORCESTERSHIRE ACUTE HOSPITALS NHS TRUST
RWW	NORTH CHESHIRE HOSPITALS NHS TRUST
RWY	CALDERDALE AND HUDDERSFIELD NHS FOUNDATION TRUST
RX1	NOTTINGHAM UNIVERSITY HOSPITALS NHS TRUST
RXC	EAST SUSSEX HOSPITALS NHS TRUST
RXF	MID YORKSHIRE HOSPITALS NHS TRUST
RXH	BRIGHTON AND SUSSEX UNIVERSITY HOSPITALS NHS TRUST
RXK	SANDWELL AND WEST BIRMINGHAM HOSPITALS NHS TRUST
RXL	BLACKPOOL, FYLDE AND WYRE HOSPITALS NHS FOUNDATION TRUST
RXN	LANCASHIRE TEACHING HOSPITALS NHS FOUNDATION TRUST
RXP	COUNTY DURHAM AND DARLINGTON NHS FOUNDATION TRUST
RXQ	BUCKINGHAMSHIRE HOSPITALS NHS TRUST
RXR	EAST LANCASHIRE HOSPITALS NHS TRUST
RXW	SHREWSBURY AND TELFORD HOSPITAL NHS TRUST
RYJ	IMPERIAL COLLEGE HEALTHCARE NHS TRUST
RBQ	**The Cardiothoracic Centre - Liverpool NHS Trust**
RPY	**The Royal Marsden NHS FD Trust**

Appendix 7.3 Describe the OG cancer ICD-10 codes used in this study

ICD10	Code description
C150	Malignant neoplasm of cervical part of oesophagus
C151	Malignant neoplasm of thoracic part of oesophagus
C152	Malignant neo of abdominal part of oesophagus
C153	Malignant neoplasm of UPPER third of oesophagus
C154	Malignant neoplasm of MID third of oesophagus
C155	Malignant neoplasm of lower third of oesophagus
C158	Malignant neoplasm overlapping lesion of oesophagus
C159	Malignant neoplasm of oesophagus unspecified
C160	Malignant neoplasm of cardia of stomach
C161	Malignant neoplasm of fundus of stomach
C162	Malignant neoplasm of body of stomach
C163	Malignant neoplasm of pyloric antrum
C164	Malignant neoplasm of pylorus
C165	Malignant neoplasm of lesser curvature of stomach
C166	Malignant neoplasm of greater curvature of stomach
C168	Malignant neoplasm overlapping lesion of stomach
C169	Malignant neoplasm of stomach unspecified

Appendix 7.4 The diagnostic gastroscopy procedure OPCS-4 codes used in this study

OPCS-4 Code	Code description
G16	Diagnostic fibreoptic endoscopic examination of oesophagus
G161	Diagnostic fibreoptic endoscopic examination of oesophagus and biopsy of lesion of oesophagus
G168	Other specified diagnostic fibreoptic endoscopic examination of oesophagus
G169	Unspecified diagnostic fibreoptic endoscopic examination of oesophagus
G45	Diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract
G451	Fibreoptic endoscopic examination of upper gastrointestinal tract and biopsy of lesion of upper gastrointestinal tract
G454	Fibreoptic endoscopic examination of upper gastrointestinal tract and staining of gastric mucosa
G458	Other specified diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract
G459	Unspecified diagnostic fibreoptic endoscopic examination of upper gastrointestinal tract

Appendix 7.5 Charlson Index of Comorbidity weights and codes.[269]

Condition	Weights	ICD10 codes
Acute myocardial infarction	1	I21, I22, I252
Congestive heart failure	1	I50
Peripheral vascular disease	1	I71, I790, I739, R02, Z958, Z959
Cerebral vascular accident	1	I60, I61, I62, I63, I65, I66, G450, G451, G452, G458, G459, G46, I64, G454, I670, I671, I672, I674, I675, I676, I677, I678, I679, I681, I682, I688, I69
Dementia	1	F00, F01, F02, F051
Pulmonary disease	1	J40, J41, J42, J44, J43, J45, J46, J47, J67, J44, J60, J61, J62, J63, J66, J64, J65
Connective tissue disorder	1	M32, M34, M332, M053, M058, M059, M060, M063, M069, M050, M052, M051, M353
Peptic ulcer	1	K25, K26, K27, K28
Liver disease	1	K702, K703, K73, K717, K740, K742, K746, K743, K744, K745
Diabetes	1	E109, E119, E139, E149, E101, E111, E131, E141, E105, E115, E135, E145
Diabetes complications	2	E102, E112, E132, E142 E103, E113, E133, E143 E104, E114, E134, E144
Paraplegia	2	G81 G041, G820, G821, G822
Renal disease	2	N03, N052, N053, N054, N055, N056, N072, N073, N074, N01, N18, N19, N25
Cancer	2	C0, C1, C2, C3, C40, C41, C43, C45, C46, C47, C48, C49, C5, C6, C70, C71, C72, C73, C74, C75, C76, C81, C82, C83, C84, C85, C883, C887, C889, C900, C901, C91, C92, C93, C940, C941, C942, C943, C9451, C947, C95, C96
Metastatic cancer	3	C77, C78, C79, C80
Severe liver disease	3	K729, K766, K767, K721
HIV	6	B20, B21, B22, B23, B24

Appendix 7.6 the adapted version of ICD10 comorbidity codes those were originally developed by Sundararajan et al.[269, 270]

	Code descriptions
I210	Acute transmural myocardial infarction of
I211	Acute transmural myocardial infarction of inferior
I212	Acute transmural myocardial infarction of other
I213	Acute transmural myocardial infarction of
I214	Acute subendocardial myocardial infarction
I219	Acute myocardial infarction unspecified
I220	Subsequent myocardial infarction of anterior wall
I221	Subsequent myocardial infarction of inferior wall
I228	Subsequent myocardial infarction of other sites
I229	Subsequent myocardial infarction of unspecified
I252	Old myocardial infarction
I500	Congestive heart failure
I501	Left ventricular failure
I509	Heart failure unspecified
I710	Dissection of aorta [any part]
I711	Thoracic aortic aneurysm ruptured
I712	Thoracic aortic aneurysm without mention of
I713	Abdominal aortic aneurysm ruptured
I714	Abdominal aortic aneurysm without mention of
I715	Thoracoabdominal aortic aneurysm ruptured
I716	Thoracoabdominal aortic aneurysm without
I718	Aortic aneurysm of unspecified site ruptured
I719	Aortic aneurysm of unspec site without mention
I790	Aneurysm of aorta in diseases classified
I739	Peripheral vascular disease unspecified
R02	Gangrene not elsewhere classified
Z95	Presence of other cardiac and vascular implants
Z95	Presence of cardiac and vascular implant and
I601	Subarachnoid haemorrhage from middle cerebral
I602	Subarachnoid haemorrhage from anterior
I603	Subarachnoid haemorrhage from posterior
I604	Subarachnoid haemorrhage from basilar artery
I605	Subarachnoid haemorrhage from vertebral artery
I606	Subarachnoid haemorrhage from other
I607	Subarachnoid haemorrhage from intracranial
I608	Other subarachnoid haemorrhage
I609	Subarachnoid haemorrhage unspecified
I610	Intracerebral haemorrhage in hemisphere
I611	Intracerebral haemorrhage in hemisphere
I612	Intracerebral haemorrhage in hemisphere
I613	Intracerebral haemorrhage in brain stem
I614	Intracerebral haemorrhage in cerebellum
I615	Intracerebral haemorrhage intraventricular
I616	Intracerebral haemorrhage multiple localized
I618	Other intracerebral haemorrhage
I619	Intracerebral haemorrhage unspecified
I620	Subdural haemorrhage (acute)(nontraumatic)
I621	Nontraumatic extradural haemorrhage
I629	Intracranial haemorrhage (nontraumatic)
I630	Cerebral infarct due to thrombosis of precerebral
I631	Cerebral infarction due to embolism of
I632	Cereb infarct due unsp occlusion or stenos
I633	Cerebral infarction due to thrombosis of cerebral
I634	Cerebral infarction due to embolism of cerebral
I635	Cerebrl infarct due unspec occlusion or stenos
I636	Cereb infarct due cerebral venous thrombosis
I638	Other cerebral infarction
I639	Cerebral infarction unspecified
I650	Occlusion and stenosis of vertebral artery
I651	Occlusion and stenosis of basilar artery
I652	Occlusion and stenosis of carotid artery
I653	Occlusion and stenosis of multip and bilat
I658	Occlusion and stenosis of other precerebral
I659	Occlusion and stenosis of unspecified precerebral
I660	Occlusion and stenosis of middle cerebral artery
I661	Occlusion and stenosis of anterior cerebral artery
I662	Occlusion and stenosis of posterior cerebral
I663	Occlusion and stenosis of cerebellar arteries
I664	Occlusion and stenosis of multiple and bilat
I668	Occlusion and stenosis of other cerebral artery
I669	Occlusion and stenosis of unspecified cerebral
G45	Vertebro-basilar artery syndrome
G45	Carotid artery syndrome (hemispheric)
G45	Multiple and bilateral precerebral artery
G45	Other transient cerebral ischaemic attacks and
G45	Transient cerebral ischaemic attack unspecified
G46	Middle cerebral artery syndrome
G46	Anterior cerebral artery syndrome
G46	Posterior cerebral artery syndrome
G46	Brain stem stroke syndrome
G46	Cerebellar stroke syndrome
G46	Pure motor lacunar syndrome
G46	Pure sensory lacunar syndrome
G46	Other lacunar syndromes
G46	Oth vascular syndromes of brain in
G45	Transient global amnesia
I64	Stroke not specified as haemorrhage or
I670	Dissection of cerebral arteries nonruptured
I671	Cerebral aneurysm nonruptured
I672	Cerebral atherosclerosis
I674	Hypertensive encephalopathy
I675	Moyamoya disease
I676	Nonpyogenic thrombosis of intracranial venous
I677	Cerebral arteritis not elsewhere classified
I678	Other specified cerebrovascular diseases
I679	Cerebrovascular disease unspecified
I681	Cerebral arteritis in infect & parasit dis classif
I682	Cerebral arteritis in other diseases classified
I688	Other cerebrovascular disorders in diseases EC
I690	Sequelae of subarachnoid haemorrhage
I691	Sequelae of intracerebral haemorrhage
I692	Sequelae of other nontraumatic intracranial
I693	Sequelae of cerebral infarction
I694	Sequelae of stroke not spec as haemorrhage or
I698	Sequelae of other and unspecified
F00	Dementia in Alzheimer s disease with early onset
F00	Dementia in Alzheimer s disease with late onset
F00	Dementia in Alzheimer s disease atypical or
F00	Dementia in Alzheimer s disease unspecified
F01	Vascular dementia of acute onset
F01	Multi-infarct dementia

F01	Subcortical vascular dementia
F01	Mixed cortical and subcortical vascular dementia
F01	Other vascular dementia
F01	Vascular dementia unspecified
F02	Dementia in Pick s disease
F02	Dementia in Creutzfeldt-Jakob disease
F02	Dementia in Huntington s disease
F02	Dementia in Parkinson s disease
F02	Dementia in human immunodef virus [HIV]
F02	Dementia in other specified diseases classified
F05	Delirium superimposed on dementia
J40	Bronchitis not specified as acute or chronic
J41	Simple chronic bronchitis
J41	Mucopurulent chronic bronchitis
J41	Mixed simple and mucopurulent chronic
J42	Unspecified chronic bronchitis
J43	MacLeod s syndrome
J43	Panlobular emphysema
J43	Centrilobular emphysema
J43	Other emphysema
J43	Emphysema unspecified
J44	Chronic obstruct pulmonary dis with acute lower
J44	Chron obstruct pulmonary dis wth acute
J44	Other specified chronic obstructive pulmonary
J44	Chronic obstructive pulmonary disease
J45	Predominantly allergic asthma
J45	Nonallergic asthma
J45	Mixed asthma
J45	Asthma unspecified
J46	Status asthmaticus
J47	Bronchiectasis
J60	Coalworker s pneumoconiosis
J61	Pneumoconiosis due to asbestos and other
J62	Pneumoconiosis due to talc dust
J62	Pneumoconiosis due to other dust containing
J63	Aluminosis (of lung)
J63	Bauxite fibrosis (of lung)
J63	Berylliosis
J63	Graphite fibrosis (of lung)
J63	Siderosis
J63	Stannosis
J63	Pneumoconiosis due to other specified inorganic
J64	Unspecified pneumoconiosis
J65	Pneumoconiosis associated with tuberculosis
J66	Byssinosis
J66	Flax-dresser s disease
J66	Cannabinosis
J66	Airway disease due to other specific organic
M3	Drug-induced systemic lupus erythematosus
M3	Systemic lupus erythematosus with organ or sys
M3	Other forms of systemic lupus erythematosus
M3	Systemic lupus erythematosus unspecified
M3	Progressive systemic sclerosis
M3	CR(E)ST syndrome
M3	Systemic sclerosis induced by drugs and
M3	Other forms of systemic sclerosis
M3	Systemic sclerosis unspecified
M3	Polymyositis
M0	Rheumatoid arthritis with involvement of oth
M0	Other seropositive rheumatoid arthritis
M0	Seropositive rheumatoid arthritis unspecified
M0	Seronegative rheumatoid arthritis
M0	Rheumatoid nodule
M0	Rheumatoid arthritis unspecified
M0	Felty s syndrome
M0	Rheumatoid vasculitis
M0	Rheumatoid lung disease
M3	Polymyalgia rheumatica
K25	Gastric ulcer acute with haemorrhage
K25	Gastric ulcer acute with perforation
K25	Gastric ulcer acute with both haemorrhage and
K25	Gastric ulcer acute without haemorrhage or
K25	Gastric ulcer chronic or unspecified with
K25	Gastric ulcer chronic or unspecified with
K25	Chronic or unspecified with both haemorrhage
K25	Gastric ulcer chronic without haemorrhage or
K25	Unspec as acute or chronic w out haemorrhage
K26	Duodenal ulcer acute with haemorrhage
K26	Duodenal ulcer acute with perforation
K26	Duodenal ulcer acute with both haemorrhage
K26	Duodenal ulcer acute without haemorrhage or
K26	Duodenal ulcer chronic or unspecified with
K26	Duodenal ulcer chronic or unspecified with
K26	Chronic or unspecified with both haemorrhage
K26	Duodenal ulcer chronic without haemorrhage or
K26	Unspec as acute or chronic w out haemorrhage
K27	Peptic ulcer acute with haemorrhage
K27	Peptic ulcer acute with perforation
K27	Peptic ulcer acute with both haemorrhage and
K27	Peptic ulcer acute without haemorrhage or
K27	Peptic ulcer chronic or unspecified with
K27	Peptic ulcer chronic or unspecified with
K27	Chronic or unspecified with both haemorrhage
K27	Peptic ulcer chronic without haemorrhage or
K27	Unspec as acute or chronic w out haemorrhage
K28	Gastrojejunal ulcer acute with haemorrhage
K28	Gastrojejunal ulcer acute with perforation
K28	Acute with both haemorrhage and perforation
K28	Acute without haemorrhage or perforation
K28	Gastrojejunal ulcer chronic or unspecified with
K28	Gastrojejunal ulcer chronic or unspecified with
K28	Chronic or unspecified with both haemorrhage
K28	Chronic without haemorrhage or perforation
K28	Unspec as acute or chronic w out haemorrhage
K70	Alcoholic fibrosis and sclerosis of liver
K70	Alcoholic cirrhosis of liver
K73	Chronic lobular hepatitis not elsewhere classified
K73	Chronic active hepatitis not elsewhere classified
K73	Other chronic hepatitis not elsewhere classified
K73	Chronic hepatitis unspecified
K71	Toxic liver disease with fibrosis and cirrhosis of
K74	Hepatic fibrosis
K74	Hepatic fibrosis with hepatic sclerosis
K74	Other and unspecified cirrhosis of liver
K74	Primary biliary cirrhosis
K74	Secondary biliary cirrhosis
K74	Biliary cirrhosis unspecified
E10	Insulin-dependent diabetes mellitus without
E11	Non-insulin-depend diabetes mellitus without
E13	Other specified diabetes mellitus without

E14	Unspecified diabetes mellitus without
E10	Insulin-dependent diabetes mellitus with
E11	Non-insulin-dependent diabetes mellitus with
E13	Other specified diabetes mellitus with
E14	Unspecified diabetes mellitus with ketoacidosis
E10	Insulin-dependent diabetes mellitus with periph
E11	Non-insulin-depend diabetes mellitus with periph
E13	Other specified diabetes mellitus with periph circ
E14	Unspecified diabetes mellitus with periph
E10	Insulin-dependent diabetes mellitus with renal
E11	Non-insulin-dependent diabetes mellitus with
E13	Other specified diabetes mellitus with renal
E14	Unspecified diabetes mellitus with renal
E10	Insulin-dependent diabetes mellitus with
E11	Non-insulin-dependent diabetes mellitus with
E13	Other specified diabetes mellitus with
E14	Unspecified diabetes mellitus with ophthalmic
E10	Insulin-dependent diabetes mellitus with
E11	Non-insulin-dependent diabetes mellitus with
E13	Other specified diabetes mellitus with
E14	Unspecified diabetes mellitus with neurological
G81	Flaccid hemiplegia
G81	Spastic hemiplegia
G81	Hemiplegia unspecified
G04	Tropical spastic paraplegia
G82	Flaccid paraplegia
G82	Spastic paraplegia
G82	Paraplegia unspecified
N03	Focal and segmental glomerular lesions
N03	Diffuse membranous glomerulonephritis
N03	Diffuse mesangial proliferative
N03	Diffuse endocapillary proliferative
N03	Diffuse mesangiocapillary glomerulonephritis
N03	Chronic nephritic syndrome dense deposit
N03	Diffuse concentric glomerulonephritis
N03	Chronic nephritic syndrome other
N03	Chronic nephritic syndrome unspecified
N05	Diffuse membranous glomerulonephritis
N05	Diffuse mesangial proliferative
N05	Diffuse endocapillary proliferative
N05	Diffuse mesangiocapillary glomerulonephritis
N05	Unspecified nephritic syndrome dense deposit
N07	Diffuse membranous glomerulonephritis
N07	Diffuse mesangial proliferative
N07	Diffuse endocapillary proliferative
N01	Minor glomerular abnormality
N01	Focal and segmental glomerular lesions
N01	Diffuse membranous glomerulonephritis
N01	Diffuse mesangial proliferative
N01	Diffuse endocapillary proliferative
N01	Diffuse mesangiocapillary glomerulonephritis
N01	Dense deposit disease
N01	Diffuse concentric glomerulonephritis
N01	Rapidly progressive nephritic syndrome other
N01	Rapidly progressive nephritic syndrome
N18	End-stage renal disease
N18	Other chronic renal failure
N18	Chronic renal failure unspecified
N19	Unspecified renal failure
N25	Renal osteodystrophy

N25	Nephrogenic diabetes insipidus
N25	Other disorders resulting from impaired renal
N25	Disorder result from impaired renal tubular
C00	Malignant neoplasm of external upper lip
C00	Malignant neoplasm of external lower lip
C00	Malignant neoplasm of external lip unspecified
C00	Malignant neoplasm of upper lip inner aspect
C00	Malignant neoplasm of lower lip inner aspect
C00	Malignant neoplasm of lip unspecified inner
C00	Malignant neoplasm of commissure of lip
C00	Malignant neoplasm of overlapping lesion of lip
C00	Malignant neoplasm of lip unspecified
C01	Malignant neoplasm of base of tongue
C02	Malignant neoplasm of dorsal surface tongue
C02	Malignant neoplasm of border of tongue
C02	Malignant neoplasm of ventral surface of tongue
C02	Malignant neo of anterior two-thirds of tongue
C02	Malignant neoplasm of lingual tonsil
C02	Malignant neoplasm of overlapping lesion of
C02	Malignant neoplasm of tongue unspecified
C03	Malignant neoplasm of upper gum
C03	Malignant neoplasm of lower gum
C03	Malignant neoplasm of gum unspecified
C04	Malignant neoplasm of floor of anterior floor of
C04	Malignant neoplasm of lateral floor of mouth
C04	Malignant neoplasm overlapping lesion of floor
C04	Malignant neoplasm of floor of mouth floor of
C05	Malignant neoplasm of hard palate
C05	Malignant neoplasm of soft palate
C05	Malignant neoplasm of uvula
C05	Malignant neoplasm overlapping lesion of palate
C05	Malignant neoplasm of palate unspecified
C06	Malignant neoplasm cheek mucosa
C06	Malignant neoplasm of vestibule of mouth
C06	Malignant neoplasm of retromolar area
C06	Malignant neoplasm overlap les of oth & unsp
C06	Malignant neoplasm of part of mouth
C07	Malignant neoplasm of parotid gland
C08	Malignant neoplasm of submandibular gland
C08	Malignant neoplasm of sublingual gland
C08	Malignant neoplasm overlapping lesion of major
C08	Malignant neoplasm of major salivary gland
C09	Malignant neoplasm tonsillar fossa
C09	Malig neo of tonsillar pillar (anterior)(posterior)
C09	Malignant neoplasm of overlapping lesion of
C09	Malignant neoplasm of tonsil unspecified
C10	Malignant neoplasm of vallecula
C10	Malignant neoplasm of anterior surface of
C10	Malignant neoplasm of lateral wall of oropharynx
C10	Malignant neoplasm of posterior wall of
C10	Malignant neoplasm of branchial cleft
C10	Malignant neoplasm overlapping lesion of
C10	Malignant neoplasm of oropharynx unspecified
C11	Malignant neoplasm of superior wall of
C11	Malignant neoplasm of posterior wall of
C11	Malignant neoplasm of lateral wall of
C11	Malignant neoplasm of anterior wall of
C11	Malignant neoplasm overlapping lesion of
C11	Malignant neoplasm of nasopharynx unspecified
C12	Malignant neoplasm of pyriform sinus

C13	Malignant neoplasm of hypopharynx postcricoid
C13	Malig neoplasm aryepiglottic fold
C13	Malignant neoplasm posterior wall of
C13	Malignant neoplasm overlapping lesion of
C13	Malignant neoplasm of hypopharynx unspecified
C14	Malignant neoplasm of pharynx unsp
C14	Malignant neoplasm of Waldeyer s ring
C14	Malig neo overlapping lesion of lip oral cavity &
C17	Malignant neoplasm of small intestine
C17	Malignant neoplasm of small intestine jejunum
C17	Malignant neoplasm of small intestine ileum
C17	Malignant neoplasm of small intestine Meckel s
C17	Malignant neoplasm overlapping lesion of small
C17	Malignant neoplasm of small intestine
C18	Malignant neoplasm of caecum
C18	Malignant neoplasm of appendix
C18	Malignant neoplasm of ascending colon
C18	Malignant neoplasm of hepatic flexure
C18	Malignant neoplasm of transverse colon
C18	Malignant neoplasm of splenic flexure
C18	Malignant neoplasm of descending colon
C18	Malignant neoplasm of sigmoid colon
C18	Malignant neoplasm overlapping lesion of colon
C18	Malignant neoplasm of colon unspecified
C19	Malignant neoplasm of rectosigmoid junction
C20	Malignant neoplasm of rectum
C21	Malignant neoplasm of anus unspecified
C21	Malignant neoplasm of anal canal
C21	Malignant neoplasm of cloacogenic zone
C21	Malig neo overlapping lesion of rectum anus
C22	Malignant neoplasm liver cell carcinoma
C22	Malignant neoplasm intrahep bile duct
C22	Malignant neoplasm hepatoblastoma
C22	Malignant neoplasm angiosarcoma of liver
C22	Malignant neoplasm other sarcomas of liver
C22	Malignant neoplasm oth spec carcinomas of liver
C22	Malignant neoplasm liver unspecified
C23	Malignant neoplasm of gallbladder
C24	Malignant neoplasm of extrahepatic bile duct
C24	Malignant neoplasm of Ampulla of Vater
C24	Malignant neoplasm overlapping lesion of biliary
C24	Malignant neoplasm of biliary tract unspecified
C25	Malignant neoplasm of head of pancreas
C25	Malignant neoplasm of body of pancreas
C25	Malignant neoplasm of tail of pancreas
C25	Malignant neoplasm of pancreatic duct
C25	Malignant neoplasm of endocrine pancreas
C25	Malignant neoplasm of other parts of pancreas
C25	Malignant neoplasm overlapping lesion of
C25	Malignant neoplasm of pancreas unspecified
C26	Malignant neoplasm of intestinal tract part unsp
C26	Malignant neoplasm of spleen
C26	Malignant neoplasm overlapping lesion of
C26	Malignant neoplasm of ill-def sites within
C30	Malignant neoplasm of nasal cavity
C30	Malignant neoplasm of middle ear
C31	Malignant neoplasm of maxillary sinus
C31	Malignant neoplasm of ethmoidal sinus
C31	Malignant neoplasm of frontal sinus
C31	Malignant neoplasm of sphenoidal sinus
C31	Malignant neoplasm overlapping lesion
C31	Malignant neoplasm of accessory sinus unsp
C32	Malignant neoplasm of glottis
C32	Malignant neoplasm of supraglottis
C32	Malignant neoplasm of subglottis
C32	Malignant neoplasm of laryngeal cartilage
C32	Malignant neoplasm overlapping lesion of larynx
C32	Malignant neoplasm of larynx unspecified
C33	Malignant neoplasm of trachea
C34	Malignant neoplasm of main bronchus
C34	Malignant neoplasm of upper lobe bronchus or
C34	Malignant neoplasm of middle lobe bronchus or
C34	Malignant neoplasm of lower lobe bronchus or
C34	Malignant neoplasm of overlap les of bronchus &
C34	Malignant neoplasm of bronchus or lung unspec
C37	Malignant neoplasm of thymus
C38	Malignant neoplasm of heart mediastinum &
C38	Malignant neoplasm of anterior mediastinum
C38	Malignant neoplasm of posterior mediastinum
C38	Malig neo heart mediastinum & pleura
C38	Malignant neoplasm of pleura
C38	Malig neo overlapping lesion of heart
C39	Malignant neoplasm of upper respiratory tract
C39	Malignant neoplasm overlap lesion of resp &
C39	Malignant neoplasm of ill-def sites within the
C40	Malignant neoplasm of scapula and long bones of
C40	Malignant neoplasm of short bones of upper limb
C40	Malignant neoplasm of long bones of lower limb
C40	Malignant neoplasm of short bones of lower limb
C40	Malignant neoplasm overlap les bone and artic
C40	Malignant neoplasm of bone and artic cart of
C41	Malignant neoplasm of bones of skull and face
C41	Malignant neoplasm of mandible
C41	Malignant neoplasm of vertebral column
C41	Malignant neoplasm of ribs sternum and clavicle
C41	Malignant neoplasm of sacrum and coccyx
C41	Malignant neoplasm overlap lesion bon and
C41	Malignant neoplasm of bone and articular
C43	Malignant melanoma of lip
C43	Malignant melanoma of eyelid including canthus
C43	Malignant melanoma of ear and ext auricular
C43	Malignant melanoma of other and unspecified
C43	Malignant melanoma of scalp and neck
C43	Malignant melanoma of trunk
C43	Malignant melanoma of upper limb including
C43	Malignant melanoma of lower limb including hip
C43	Malignant melanoma of skin
C43	Malignant melanoma of skin unsp
C45	Mesothelioma of pleura
C45	Mesothelioma of peritoneum
C45	Mesothelioma of pericardium
C45	Mesothelioma of other sites
C45	Mesothelioma unspecified
C46	Kaposi s sarcoma of skin
C46	Kaposi s sarcoma of soft tissue
C46	Kaposi s sarcoma of palate
C46	Kaposi s sarcoma of lymph nodes
C46	Kaposi s sarcoma of other sites
C46	Kaposi s sarcoma of multiple organs
C46	Kaposi s sarcoma unspecified

C47	Malignant neoplasm of peripheral nerve of head
C47	Malignant neoplasm of peripheral nerve upp limb
C47	Malignant neoplasm of peripheral nerve of low
C47	Malignant neoplasm of peripheral nerve of
C47	Malignant neoplasm of peripheral nerve of
C47	Malignant neoplasm of peripheral nerve of pelvis
C47	Malignant neoplasm of peripheral nerve of trunk
C47	Malignant neoplasm overlap lesion periph nerve
C47	Malignant neoplasm periph nerve & autonomic
C48	Malignant neoplasm of retroperitoneum
C48	Malignant neoplasm of spec parts of peritoneum
C48	Malignant neoplasm of peritoneum unsp
C48	Malignant neoplasm of overlap lesion retroperit
C49	Malignant neoplasm of conn and soft tiss head
C49	Malignant neoplasm of conn and soft tiss upp
C49	Malignant neoplasm of conn and soft tiss lower
C49	Malignant neoplasm of conn and soft tiss of
C49	Malignant neoplasm of conn and soft tiss of
C49	Malignant neoplasm of conn and soft tiss of
C49	Malignant neoplasm of conn and soft tiss of trunk
C49	Malignant neoplasm overlap lesion connective &
C49	Malignant neoplasm of connective and soft tissue
C50	Malignant neoplasm of nipple and areola
C50	Malignant neoplasm of central portion of breast
C50	Malignant neoplasm of upper-inner quadrant of
C50	Malignant neoplasm of lower-inner quadrant of
C50	Malignant neoplasm of upper-outer quadrant of
C50	Malignant neoplasm of lower-outer quadrant of
C50	Malignant neoplasm of axillary tail of breast
C50	Malignant neoplasm overlapping lesion of breast
C50	Malignant neoplasm of breast unspecified
C51	Malignant neoplasm of labium majus
C51	Malignant neoplasm of labium minus
C51	Malignant neoplasm of clitoris
C51	Malignant neoplasm of overlapping lesion of
C51	Malignant neoplasm of vulva unspecified
C52	Malignant neoplasm of vagina
C53	Malignant neoplasm of endocervix
C53	Malignant neoplasm of exocervix
C53	Malignant neoplasm overlapping lesion of cervix
C53	Malignant neoplasm of cervix uteri unsp
C54	Malignant neoplasm of isthmus uteri
C54	Malignant neoplasm of endometrium
C54	Malignant neoplasm of myometrium
C54	Malignant neoplasm of fundus uteri
C54	Malignant neoplasm overlapping lesion of corpus
C54	Malignant neoplasm of corpus uteri unsp
C55	Malignant neoplasm of uterus part unspecified
C56	Malignant neoplasm of ovary
C57	Malignant neoplasm of fallopian tube
C57	Malignant neoplasm of broad ligament
C57	Malignant neoplasm of round ligament
C57	Malignant neoplasm of parametrium
C57	Malignant neoplasm of uterine adnexa unsp
C57	Malignant neoplasm of other specified female
C57	Malignant neoplasm overlapping lesion female
C57	Malignant neoplasm of female genital organ
C58	Malignant neoplasm of placenta
C60	Malignant neoplasm of prepuce
C60	Malignant neoplasm of glans penis
C60	Malignant neoplasm of body of penis
C60	Malignant neoplasm overlapping lesion of penis
C60	Malignant neoplasm of penis unspecified
C61	Malignant neoplasm of prostate
C62	Malignant neoplasm of undescended testis
C62	Malignant neoplasm of descended testis
C62	Malignant neoplasm of testis unspecified
C63	Malignant neoplasm of epididymis
C63	Malignant neoplasm of spermatic cord
C63	Malignant neoplasm of scrotum
C63	Malignant neoplasm of other specified male
C63	Malignant neoplasm overlapping lesion male
C63	Malignant neoplasm of male genital organ
C64	Malignant neoplasm of kidney except renal
C65	Malignant neoplasm of renal pelvis
C66	Malignant neoplasm of ureter
C67	Malignant neoplasm of trigone of bladder
C67	Malignant neoplasm of dome of bladder
C67	Malignant neoplasm of lateral wall of bladder
C67	Malignant neoplasm of anterior wall of bladder
C67	Malignant neoplasm of posterior wall of bladder
C67	Malignant neoplasm of bladder neck
C67	Malignant neoplasm of ureteric orifice
C67	Malignant neoplasm of urachus
C67	Malignant neoplasm overlapping lesion of
C67	Malignant neoplasm of bladder unspecified
C68	Malignant neoplasm of urethra
C68	Malignant neoplasm of paraurethral gland
C68	Malignant neoplasm of overlapping lesion urinary
C68	Malignant neoplasm of urinary organ unspecified
C69	Malignant neoplasm of conjunctiva
C69	Malignant neoplasm of cornea
C69	Malignant neoplasm of retina
C69	Malignant neoplasm of choroid
C69	Malignant neoplasm of ciliary body
C69	Malignant neoplasm of lacrimal gland and duct
C69	Malignant neoplasm of orbit
C69	Malignant neoplasm overlapping lesion eye and
C69	Malignant neoplasm of eye unspecified
C70	Malignant neoplasm of cerebral meninges
C70	Malignant neoplasm of spinal meninges
C70	Malignant neoplasm of meninges unspecified
C71	Malignant neoplasm of cerebrum except lobes &
C71	Malignant neoplasm of cerebrum frontal lobe
C71	Malignant neoplasm of cerebrum temporal lobe
C71	Malignant neoplasm of cerebrum parietal lobe
C71	Malignant neoplasm of cerebrum occipital lobe
C71	Malignant neoplasm of cerebrum cerebral
C71	Malignant neoplasm of cerebrum cerebellum
C71	Malignant neoplasm of cerebrum brain stem
C71	Malignant neoplasm of cerebrum overlapping
C71	Malignant neoplasm of cerebrum brain
C72	Malignant neoplasm of spinal cord
C72	Malignant neoplasm of cauda equina
C72	Malignant neoplasm of Olfactory nerve
C72	Malignant neoplasm of Optic nerve
C72	Malignant neoplasm of Acoustic nerve
C72	Malignant neoplasm of other and unspecified
C72	Malignant neoplasm overlapping lesion
C72	Malignant neoplasm of Central Nervous System

C73	Malignant neoplasm of thyroid gland
C74	Malignant neoplasm of cortex of adrenal gland
C74	Malignant neoplasm of medulla of adrenal gland
C74	Malignant neoplasm of adrenal gland unsp
C75	Malignant neoplasm of parathyroid gland
C75	Malignant neoplasm of pituitary gland
C75	Malignant neoplasm of craniopharyngeal duct
C75	Malignant neoplasm of pineal gland
C75	Malignant neoplasm of carotid body
C75	Malignant neoplasm of aortic body and other
C75	Malignant neoplasm pluriglandular involvment
C75	Malignant neoplasm of endocrine gland
C76	Malignant neoplasm of head face & neck
C76	Malignant neoplasm of thorax
C76	Malignant neoplasm of abdomen
C76	Malignant neoplasm of pelvis
C76	Malignant neoplasm of upper limb
C76	Malignant neoplasm of lower limb
C76	Malignant neoplasm of other ill-defined sites
C76	Malignant neoplasm overlap lesion oth & ill-
C81	Hodgkin s disease lymphocytic predominance
C81	Hodgkin s disease nodular sclerosis
C81	Hodgkin s disease mixed cellularity
C81	Hodgkin s disease lymphocytic depletion
C81	Hodgkin s disease other Hodgkin s disease
C81	Hodgkin s disease Hodgkin s disease unspecified
C82	Follicular non-Hodgkin s small cleaved cell
C82	Follicular non-Hodg mixed sml cleavd & lge cell
C82	Follicular non-Hodgkin s large cell lymphoma
C82	Follicular non-Hodgkin s other types of
C82	Follicular non-Hodgkin s unspecified lymphoma
C83	Diffuse non-Hodgkin s small cell
C83	Diffuse non-Hodgkin s small cleaved cell (diffuse)
C83	Diffuse non-Hodgkin mixed sml & lge cell
C83	Diffuse non-Hodgkin s large cell (diffuse)
C83	Diffuse non-Hodgkin s immunoblastic (diffuse)
C83	Diffuse non-Hodgkin s lymphoblastic (diffuse)
C83	Diffuse non-Hodgkin s lymphoma
C83	Diffuse non-Hodgkin s lymphoma Burkitt s
C83	Other types of diffuse non-Hodgkin s lymphoma
C83	Diffuse non-Hodgkin s lymphoma unspecified
C84	Peripheral and cutaneous T-cell lymphomas
C84	Peripheral and cutaneous T-cell lymphomas
C84	Peripheral and cutaneous T-cell lymphomas T-
C84	Periph & cutan T-cell lymphomas
C84	Periph & cutan T-cell lymphomas peripheral T-
C84	Periph & cutan T-cell lymphomas oth & unsp T-
C85	Oth & unspec types of non-Hodgkin s lymphoma
C85	Oth & unsp types non-Hodgkin s B-cell lymphoma
C85	Oth specified types of non-Hodgkin s lymphoma
C85	Non-Hodgkin s lymphoma unspecified type
C88	Malignant immunoproliferative small intestinal
C88	Other malignant immunoproliferative diseases
C88	Malignant immunoproliferative disease
C90	Multiple myeloma
C90	Plasma cell leukaemia
C91	Acute lymphoblastic leukaemia
C91	Chronic lymphocytic leukaemia
C91	Subacute lymphocytic leukaemia
C91	Prolymphocytic leukaemia
C91	Hairy-cell leukaemia
C91	Adult T-cell leukaemia
C91	Other lymphoid leukaemia
C91	Lymphoid leukaemia unspecified
C92	Acute myeloid leukaemia
C92	Chronic myeloid leukaemia
C92	Subacute myeloid leukaemia
C92	Myeloid sarcoma
C92	Acute promyelocytic leukaemia
C92	Acute myelomonocytic leukaemia
C92	Other myeloid leukaemia
C92	Myeloid leukaemia unspecified
C93	Acute monocytic leukaemia
C93	Chronic monocytic leukaemia
C93	Subacute monocytic leukaemia
C93	Other monocytic leukaemia
C93	Monocytic leukaemia unspecified
C94	Acute erythraemia & erythroleukaemia
C94	Chronic erythraemia
C94	Acute megakaryoblastic leukaemia
C94	Mast cell leukaemia
C94	Acute myelofibrosis
C94	Other specified leukaemias
C95	Acute leukaemia of unsp cell type
C95	Chronic leukaemia unsp cell type
C95	Subacute leukaemia unsp cell type
C95	Other leukaemia unspecified cell type
C95	Leukaemia unspecified
C96	Letterer-Siwe disease
C96	Malignant histiocytosis
C96	Malignant mast cell tumour
C96	True histiocyt lymphoma
C96	Oth spec malig neop lymphoid h poietic & related
C96	Malig neop lymphoid haematopoietic and related
C77	Sec & uns malig neoplasm of lymph nodes of
C77	Sec & uns malignant neoplasm of intrathoracic
C77	Sec & uns malignant neoplasm of intra-
C77	Sec & uns malig neoplasm of axillary & upp limb
C77	Sec & uns malig neoplasm of inguinal & low limb
C77	Sec & uns malignant neoplasm of intrapelvic
C77	Sec & uns malig neoplasm of lymph nodes of
C77	Sec & uns malignant neoplasm of lymph node
C78	Secondary malignant neoplasm of lung
C78	Secondary malignant neoplasm of mediastinum
C78	Secondary malignant neoplasm of pleura
C78	Secondary malignant neoplasm of oth & unsp
C78	Secondary malignant neoplasm of small intestine
C78	Secondary malignant neoplasm of large intest &
C78	Secondary malignant neoplasm of
C78	Secondary malignant neoplasm of liver
C78	Secondary malignant neoplasm of other & unsp
C79	Secondary malignant neoplasm of kidney & renal
C79	Secondary malignant neoplasm of oth & uns
C79	Secondary malignant neoplasm of skin
C79	Secondary malignant neoplasm of brain &
C79	Secondary malignant neoplasm of oth & unsp
C79	Secondary malignant neoplasm of bone and bone
C79	Secondary malignant neoplasm of ovary
C79	Secondary malignant neoplasm of adrenal gland
C79	Secondary malignant neoplasm of other specified

C80	Malignant neoplasm without specification of site
K72	Hepatic failure unspecified
K76	Portal hypertension
K76	Hepatorenal syndrome
K72	Chronic hepatic failure
B20	HIV disease resulting in mycobacterial infection
B20	HIV disease resulting in other bacterial infections
B20	HIV disease resulting in cytomegaloviral disease
B20	HIV disease resulting in other viral infections
B20	HIV disease resulting in candidiasis
B20	HIV disease resulting in other mycoses
B20	HIV disease resulting in Pneumocystis carinii
B20	HIV disease resulting in multiple infections
B20	HIV dis resulting in oth infectious and parasitic dis
B20	HIV disease resulting in unspec infectious or
B21	HIV disease resulting in Kaposi s sarcoma
B21	HIV disease resulting in Burkitt s lymphoma

B21	HIV dis resulting oth types of non-Hodgkin s
B21	HIV dis result oth mal neo lymphoid
B21	HIV disease resulting in multiple malignant
B21	HIV disease resulting in other malignant
B21	HIV disease resulting in unspecified malignant
B22	HIV disease resulting in encephalopathy
B22	HIV disease resulting in lymphoid interstitial
B22	HIV disease resulting in wasting syndrome
B22	HIV dis resulting in multiple diseases classif
B23	Acute HIV infection syndrome
B23	HIV dis result (persistent) generalized
B23	HIV dis result haematologic / immunologic
B23	HIV disease resulting in other specified conditions
B24	Unspecified human immunodefiency virus [HIV]

Appendix 7.7 describe the OG cancer related surgical procedure OPCS-4 codes used in this study

OPCS-4 codes	Code description
G011	Oesophagogastrectomy and anastomosis of oesophagus to stomach
G012	Oesophagogastrectomy and anastomosis of oesophagus to transposed jejunum
G013	Oesophagogastrectomy and anastomosis of oesophagus to jejunum NEC
G018	Other specified excision of oesophagus and stomach
G019	Unspecified excision of oesophagus and stomach
G021	Total oesophagectomy and anastomosis of pharynx to stomach
G022	Total oesophagectomy and interposition of microvascularly attached jejunum
G023	Total oesophagectomy and interposition of jejunum NEC
G024	Total oesophagectomy and interposition of microvascularly attached colon
G025	Total oesophagectomy and interposition of colon NEC
G028	Other specified total excision of oesophagus
G029	Unspecified total excision of oesophagus
G031	Partial oesophagectomy and end to end anastomosis of oesophagus
G032	Partial oesophagectomy and interposition of microvascularly attached jejunum
G035	Partial oesophagectomy and interposition of microvascularly attached colon
G036	Partial oesophagectomy and interposition of colon NEC
G038	Other specified partial excision of oesophagus
G039	Unspecified partial excision of oesophagus
G271	Total gastrectomy and excision of surrounding tissue
G272	Total gastrectomy and anastomosis of oesophagus to duodenum
G273	Total gastrectomy and interposition of jejunum
G274	Total gastrectomy and anastomosis of oesophagus to transposed jejunum
G275	Total gastrectomy and anastomosis of oesophagus to jejunum NEC
G278	Other specified total excision of stomach
G281	Partial gastrectomy and anastomosis of stomach to duodenum
G282	Partial gastrectomy and anastomosis of stomach to transposed jejunum
G283	Partial gastrectomy and anastomosis of stomach to jejunum NEC
G288	Other specified partial excision of stomach

Appendix 7.8 Coded diagnostic profile at the first diagnostic gastroscopy procedure

	OG cancer C15, C16 ICD-10 codes
C150	Malignant neoplasm of cervical part of oesophagus
C151	Malignant neoplasm of thoracic part of oesophagus
C152	Malignant neo of abdominal part of oesophagus
C153	Malignant neoplasm of upper third of oesophagus
C154	Malignant neoplasm of middle third of oesophagus
C155	Malignant neoplasm of lower third of oesophagus
C158	Malignant neoplasm overlapping lesion of
C159	Malignant neoplasm of oesophagus unspecified
C160	Malignant neoplasm of cardia of stomach
C161	Malignant neoplasm of fundus of stomach
C162	Malignant neoplasm of body of stomach
C163	Malignant neoplasm of pyloric antrum
C164	Malignant neoplasm of pylorus
C165	Malignant neoplasm of lesser curvature of stomach,
C166	Malignant neoplasm of greater curvature of stomach,
C168	Malignant neoplasm overlapping lesion of stomach
C169	Malignant neoplasm of stomach, unspecified
	Major acid-peptic lesions
K221	Ulcer of oesophagus
K222	Oesophageal obstruction
K250	Gastric ulcer, acute with haemorrhage
K251	Gastric ulcer, acute with perforation
K252	Gastric ulcer, acute with both haemorrhage and
K253	Gastric ulcer, acute without haemorrhage or
K254	Gastric ulcer, chronic or unspecified with
K255	Gastric ulcer, chronic or unspecified with perforation
K257	Gastric ulcer, chronic without haemorrhage or
K260	Duodenal ulcer, acute with haemorrhage
K261	Duodenal ulcer, acute with perforation
K262	Duodenal ulcer, acute with both haemorrhage and
K263	Duodenal ulcer, acute without haemorrhage or
K264	Duodenal ulcer, chronic or unspecified with
K265	Duodenal ulcer, chronic or unspecified with
K267	Duodenal ulcer, chronic without haemorrhage or
K270	Peptic ulcer, acute with haemorrhage
K271	Peptic ulcer, acute with perforation
K272	Peptic ulcer, acute with both haemorrhage and
K273	Peptic ulcer, acute without haemorrhage or
K274	Peptic ulcer, chronic or unspecified with haemorrhage
K275	Peptic ulcer, chronic or unspecified with perforation
K277	Peptic ulcer, chronic without haemorrhage or
K280	Gastrojejunal ulcer, acute with haemorrhage
K284	Gastrojejunal ulcer, chronic or unspecified with
K312	Hourglass stricture and stenosis of stomach
K315	Obstruction of duodenum
Q393	Congenital stenosis and stricture of oesophagus
	Normal or minor pathologies
K20X	Oesophagitis
K210	Gastro-oesophageal reflux disease with oesophagitis
K219	Gastro-oesophageal reflux disease without
K229	Disease of oesophagus, unspecified
K230	Tuberculous oesophagitis
K291	Other acute gastritis
K292	Alcoholic gastritis
K293	Chronic superficial gastritis
K294	Chronic atrophic gastritis
K295	Chronic gastritis, unspecified
K296	Other gastritis
K297	Gastritis, unspecified
K298	Duodenitis
K299	Gastroduodenitis, unspecified
K319	Disease of stomach and duodenum, unspecified
K449	Diaphragmatic hernia without obstruction or
K458	Other spec abdom hernia without obstruction or
K469	Unspecified abdominal hernia without obstruction or
Q394	Oesophageal web
Q401	Congenital hiatus hernia
	Other neoplasms
C170	Malignant neoplasm of small intestine, duodenum
C171	Malignant neoplasm of small intestine, jejunum
C172	Malignant neoplasm of small intestine, ileum
C178	Malignant neoplasm overlapping lesion of small
C179	Malignant neoplasm of small intestine, unspecified
C180	Malignant neoplasm of caecum
C181	Malignant neoplasm of appendix
C182	Malignant neoplasm of ascending colon
C183	Malignant neoplasm of hepatic flexure
C184	Malignant neoplasm of transverse colon
C186	Malignant neoplasm of descending colon
C188	Malignant neoplasm overlapping lesion of colon
C189	Malignant neoplasm of colon, unspecified
C19X	Malignant neoplasm of rectosigmoid junction
C20X	Malignant neoplasm of rectum
C210	Malignant neoplasm of anus, unspecified
C211	Malignant neoplasm of anal canal
C220	Malignant neoplasm, liver cell carcinoma
C221	Malignant neoplasm, intrahep bile duct carcinoma
C222	Malignant neoplasm, hepatoblastoma
C227	Malignant neoplasm, oth spec carcinomas of liver
C229	Malignant neoplasm, liver, unspecified
C23X	Malignant neoplasm of gallbladder
C240	Malignant neoplasm of extrahepatic bile duct
C241	Malignant neoplasm of Ampulla of Vater
C248	Malignant neoplasm overlapping lesion of biliary tract
C249	Malignant neoplasm of biliary tract, unspecified
C250	Malignant neoplasm of head of pancreas
C251	Malignant neoplasm of body of pancreas
C252	Malignant neoplasm of tail of pancreas
C253	Malignant neoplasm of pancreatic duct
C257	Malignant neoplasm of other parts of pancreas
C258	Malignant neoplasm, overlapping lesion of pancreas
C259	Malignant neoplasm of pancreas, unspecified
C260	Malignant neoplasm of intestinal tract, part unsp
C268	Malignant neoplasm, overlapping lesion of digestive
C269	Malignant neoplasm of ill-def sites within digestive
C481	Malignant neoplasm of spec parts of peritoneum
C784	Secondary malignant neoplasm of small intestine
C785	Secondary malignant neoplasm of large intest &
C787	Secondary malignant neoplasm of liver
C788	Secondary malignant neoplasm of other & unsp
C883	Malignant immunoproliferative small intestinal
D010	Carcinoma in situ colon
D011	Carcinoma in situ rectosigmoid junction
D012	Carcinoma in situ rectum

D013	Carcinoma in situ anus and anal canal
D014	Carcinoma in situ other and unspecified parts of
D015	Carcinoma in situ liver, gallbladder and bile ducts
D017	Carcinoma in situ other specified digestive organs
D120	Benign neoplasm of caecum
D121	Benign neoplasm of appendix
D122	Benign neoplasm of ascending colon
D123	Benign neoplasm of transverse colon
D125	Benign neoplasm of sigmoid colon
D126	Benign neoplasm of colon, unspecified
D128	Benign neoplasm of rectum
D129	Benign neoplasm of anus and anal canal
D133	Benign neoplasm of other and unsp parts of small
D134	Benign neoplasm of liver
D135	Benign neoplasm of extrahepatic bile ducts
D136	Benign neoplasm of pancreas
D137	Benign neoplasm of endocrine pancreas
D139	Benign neoplasm of ill-defined site within the
D152	Benign neoplasm of mediastinum
D175	Benign lipomatous neoplasm of intra-abdominal
D214	Benign neoplasm of conn & soft tiss of abdomen
D372	Neoplasm uncert / unkn behav small intestine
D374	Neoplasm uncert / unkn behav colon
D375	Neoplasm uncert / unkn behav rectum
B217	HIV disease resulting in multiple malignant neoplasms
B218	HIV disease resulting in other malignant neoplasms
C01X	Malignant neoplasm of base of tongue
C020	Malignant neoplasm of dorsal surface tongue
C021	Malignant neoplasm of border of tongue
C022	Malignant neoplasm of ventral surface of tongue
C024	Malignant neoplasm of lingual tonsil
C028	Malignant neoplasm of overlapping lesion of tongue
C029	Malignant neoplasm of tongue, unspecified
C031	Malignant neoplasm of lower gum
C040	Malignant neoplasm of floor of anterior floor of
C048	Malignant neoplasm, overlapping lesion of floor of
C049	Malignant neoplasm of floor of mouth, floor of
C050	Malignant neoplasm of hard palate
C051	Malignant neoplasm of soft palate
C052	Malignant neoplasm of uvula
C058	Malignant neoplasm, overlapping lesion of palate
C059	Malignant neoplasm of palate, unspecified
C060	Malignant neoplasm cheek mucosa
C062	Malignant neoplasm of retromolar area
C068	Malignant neoplasm, overlap les of oth & unsp part of
C069	Malignant neoplasm of part of mouth, unspecified
C07X	Malignant neoplasm of parotid gland
C080	Malignant neoplasm of submandibular gland
C089	Malignant neoplasm of major salivary gland,
C090	Malignant neoplasm tonsillar fossa
C091	Malig neo of tonsillar pillar (anterior)(posterior)
C098	Malignant neoplasm of overlapping lesion of tonsil
C099	Malignant neoplasm of tonsil unspecified
C100	Malignant neoplasm of vallecula
C101	Malignant neoplasm of anterior surface of epiglottis
C102	Malignant neoplasm of lateral wall of oropharynx
C103	Malignant neoplasm of posterior wall of oropharynx
C109	Malignant neoplasm of oropharynx unspecified
C111	Malignant neoplasm of posterior wall of nasopharynx
C112	Malignant neoplasm of lateral wall of nasopharynx
C113	Malignant neoplasm of anterior wall of nasopharynx
C119	Malignant neoplasm of nasopharynx unspecified
C12X	Malignant neoplasm of pyriform sinus
C130	Malignant neoplasm of hypopharynx, postcricoid
C131	Malig neoplasm aryepiglottic fold, hypopharyngeal
C132	Malignant neoplasm posterior wall of hypopharynx
C139	Malignant neoplasm of hypopharynx unspecified
C140	Malignant neoplasm of pharynx, unsp
C148	Malig neo, overlapping lesion of lip, oral cavity &
C185	Malignant neoplasm of splenic flexure
C187	Malignant neoplasm of sigmoid colon
C218	Malig neo, overlapping lesion of rectum, anus and
C300	Malignant neoplasm of nasal cavity
C310	Malignant neoplasm of maxillary sinus
C311	Malignant neoplasm of ethmoidal sinus
C312	Malignant neoplasm of frontal sinus
C320	Malignant neoplasm of glottis
C321	Malignant neoplasm of supraglottis
C322	Malignant neoplasm of subglottis
C323	Malignant neoplasm of laryngeal cartilage
C328	Malignant neoplasm, overlapping lesion of larynx
C329	Malignant neoplasm of larynx, unspecified
C33X	Malignant neoplasm of trachea
C340	Malignant neoplasm of main bronchus
C341	Malignant neoplasm of upper lobe, bronchus or lung
C342	Malignant neoplasm of middle lobe, bronchus or lung
C343	Malignant neoplasm of lower lobe, bronchus or lung
C348	Malignant neoplasm of overlap les of bronchus & lung
C349	Malignant neoplasm of bronchus or lung, unspec
C37X	Malignant neoplasm of thymus
C380	Malignant neoplasm of heart, mediastinum & pleura,
C381	Malignant neoplasm of anterior mediastinum
C383	Malig neo heart, mediastinum &
C384	Malignant neoplasm of pleura
C390	Malignant neoplasm of upper respiratory tract, part
C402	Malignant neoplasm of long bones of lower limb
C410	Malignant neoplasm of bones of skull and face
C411	Malignant neoplasm of mandible
C412	Malignant neoplasm of vertebral column
C433	Malignant melanoma of other and unspecified parts
C434	Malignant melanoma of scalp and neck
C435	Malignant melanoma of trunk
C436	Malignant melanoma of upper limb, including
C437	Malignant melanoma of lower limb, including hip
C439	Malignant melanoma of skin, unsp
C440	Other malignant neoplasms of skin of lip
C441	Other malignant neoplasms of skin of eyelid, incl
C443	Oth malignant neoplasm of skin of oth & unsp parts of
C444	Other malignant neoplasms of skin of scalp and neck
C445	Other malignant neoplasms of skin of trunk
C447	Other malignant neoplasms of skin of lower limb, incl
C449	Other malignant neoplasms of skin, unspecified
C450	Mesothelioma of pleura
C451	Mesothelioma of peritoneum
C457	Mesothelioma of other sites
C459	Mesothelioma, unspecified
C467	Kaposi's sarcoma of other sites
C469	Kaposi's sarcoma, unspecified
C474	Malignant neoplasm of peripheral nerve of abdomen
C480	Malignant neoplasm of retroperitoneum

C482	Malignant neoplasm of peritoneum, unsp
C490	Malignant neoplasm of conn and soft tiss head, face &
C492	Malignant neoplasm of conn and soft tiss,lower
C493	Malignant neoplasm of conn and soft tiss of thorax
C494	Malignant neoplasm of conn and soft tiss of abdomen
C495	Malignant neoplasm of conn and soft tiss of pelvis
C498	Malignant neoplasm, overlap lesion connective & soft
C499	Malignant neoplasm of connective and soft tissue,
C500	Malignant neoplasm of nipple and areola
C502	Malignant neoplasm of upper-inner quadrant of
C504	Malignant neoplasm of upper-outer quadrant of
C505	Malignant neoplasm of lower-outer quadrant of
C506	Malignant neoplasm of axillary tail of breast
C508	Malignant neoplasm, overlapping lesion of breast
C509	Malignant neoplasm of breast, unspecified
C519	Malignant neoplasm of vulva, unspecified
C52X	Malignant neoplasm of vagina
C539	Malignant neoplasm of cervix uteri, unsp
C541	Malignant neoplasm of endometrium
C549	Malignant neoplasm of corpus uteri, unsp
C55X	Malignant neoplasm of uterus, part unspecified
C56X	Malignant neoplasm of ovary
C579	Malignant neoplasm of female genital organ,
C609	Malignant neoplasm of penis, unspecified
C61X	Malignant neoplasm of prostate
C620	Malignant neoplasm of undescended testis
C621	Malignant neoplasm of descended testis
C629	Malignant neoplasm of testis, unspecified
C64X	Malignant neoplasm of kidney, except renal pelvis
C65X	Malignant neoplasm of renal pelvis
C66X	Malignant neoplasm of ureter
C671	Malignant neoplasm of dome of bladder
C672	Malignant neoplasm of lateral wall of bladder
C674	Malignant neoplasm of posterior wall of bladder
C676	Malignant neoplasm of ureteric orifice
C679	Malignant neoplasm of bladder, unspecified
C688	Malignant neoplasm of overlapping lesion urinary
C689	Malignant neoplasm of urinary organ, unspecified
C701	Malignant neoplasm of spinal meninges
C709	Malignant neoplasm of meninges, unspecified
C710	Malignant neoplasm of cerebrum, except lobes &
C711	Malignant neoplasm of cerebrum, frontal lobe
C712	Malignant neoplasm of cerebrum, temporal lobe
C713	Malignant neoplasm of cerebrum, parietal lobe
C716	Malignant neoplasm of cerebrum, cerebellum
C718	Malignant neoplasm of cerebrum, overlapping lesion
C719	Malignant neoplasm of cerebrum, brain, unspecified
C720	Malignant neoplasm of spinal cord
C73X	Malignant neoplasm of thyroid gland
C749	Malignant neoplasm of adrenal gland, unsp
C759	Malignant neoplasm of endocrine gland, unspecified
C760	Malignant neoplasm of head, face & neck
C763	Malignant neoplasm of pelvis
C767	Malignant neoplasm of other ill-defined sites
C770	Sec & uns malig neoplasm of lymph nodes of head,
C773	Sec & uns malig neoplasm of axillary & upp limb
C774	Sec & uns malig neoplasm of inguinal & low limb
C775	Sec & uns malignant neoplasm of intrapelvic lymph
C778	Sec & uns malig neoplasm of lymph nodes of multiple
C779	Sec & uns malignant neoplasm of lymph node,
C780	Secondary malignant neoplasm of lung
C781	Secondary malignant neoplasm of mediastinum
C782	Secondary malignant neoplasm of pleura
C783	Secondary malignant neoplasm of oth & unsp
C786	Secondary malignant neoplasm of retroperitoneum &
C791	Secondary malignant neoplasm of oth & uns urinary
C792	Secondary malignant neoplasm of skin
C793	Secondary malignant neoplasm of brain & cerebral
C795	Secondary malignant neoplasm of bone and bone
C796	Secondary malignant neoplasm of ovary
C797	Secondary malignant neoplasm of adrenal gland
C798	Secondary malignant neoplasm of other specified
C80X	Malignant neoplasm without specification of site
C810	Hodgkin's disease, lymphocytic predominance
C811	Hodgkin's disease, nodular sclerosis
C812	Hodgkin's disease, mixed cellularity
C817	Hodgkin's disease, other Hodgkin's disease
C819	Hodgkin's disease, Hodgkin's disease, unspecified
C822	Follicular non-Hodgkin's large cell lymphoma
C827	Follicular non-Hodgkin's other types of lymphoma
C829	Follicular non-Hodgkin's unspecified lymphoma
C830	Diffuse non-Hodgkin's small cell (diffuse)lymphoma
C833	Diffuse non-Hodgkin's large cell (diffuse) lymphoma
C835	Diffuse non-Hodgkin's lymphoblastic (diffuse)
C837	Diffuse non-Hodgkin's lymphoma, Burkitt's tumour
C838	Other types of diffuse non-Hodgkin's lymphoma
C839	Diffuse non-Hodgkin's lymphoma, unspecified
C840	Peripheral and cutaneous T-cell lymphomas, mycosis
C841	Peripheral and cutaneous T-cell lymphomas, Sezary's
C844	Periph & cutan T-cell lymphomas, peripheral T-cell
C845	Periph & cutan T-cell lymphomas, oth & unsp T-cell
C850	Oth & unspec types of non-Hodgkin's lymphoma,
C851	Oth & unsp types non-Hodgkin's B-cell lymphoma,
C857	Oth specified types of non-Hodgkin's lymphoma
C859	Non-Hodgkin's lymphoma, unspecified type
C880	Waldenstrom's macroglobulinaemia
C900	Multiple myeloma
C901	Plasma cell leukaemia
C902	Malignant plasma cell neoplasm, extramedullary
C910	Acute lymphoblastic leukaemia
C911	Chronic lymphocytic leukaemia
C913	Prolymphocytic leukaemia
C914	Hairy-cell leukaemia
C915	Adult T-cell leukaemia
C919	Lymphoid leukaemia, unspecified
C920	Acute myeloid leukaemia
C921	Chronic myeloid leukaemia
C924	Acute promyelocytic leukaemia
C925	Acute myelomonocytic leukaemia
C927	Other myeloid leukaemia
C929	Myeloid leukaemia, unspecified
C950	Acute leukaemia of unsp cell type
C951	Chronic leukaemia unsp cell type
C961	Malignant histiocytosis
C969	Malig neop lymphoid haematopoietic and related
C97X	Malignant neoplasms of independent (primary)
D000	Carcinoma in situ of lip, oral cavity and pharynx
D020	Carcinoma in situ larynx
D021	Carcinoma in situ trachea
D022	Carcinoma in situ bronchus and lung

D049	Carcinoma in situ of skin unspecified
D051	Intraductal carcinoma in situ
D059	Carcinoma in situ of breast, unspecified
D090	Carcinoma in situ of bladder
D093	Carcinoma in situ of thyroid and other endocrine
D101	Benign neoplasm of tongue
D102	Benign neoplasm of floor of mouth
D103	Benign neoplasm of other and unsp parts of mouth
D104	Benign neoplasm of tonsil
D105	Benign neoplasm of other parts of oropharynx
D106	Benign neoplasm of nasopharynx
D107	Benign neoplasm of hypopharynx
D109	Benign neoplasm of pharynx, unspecified
D110	Benign neoplasm of parotid gland
D119	Benign neoplasm of major salivary gland, unspecified
D124	Benign neoplasm of descending colon
D127	Benign neoplasm of rectosigmoid junction
D140	Benign neoplasm of mid ear, nasal cav & accessory
D141	Benign neoplasm of larynx
D143	Benign neoplasm of bronchus and lung
D157	Benign neoplasm of other specified intrathoracic
D162	Benign neoplasm of long bones of lower limb
D170	Benign lipomatous neop skin/subcut tis head face &
D171	Benign lipomatous neoplasm skin and subcut tissue of
D173	Benign lipomatous neop skin/subcut tis other/unspec
D179	Benign lipomatous neoplasm, unspecified
D180	Haemangioma, any site
D181	Lymphangioma, any site
D190	Benign neoplasm of mesothelial tissue of pleura
D191	Benign neoplasm of mesothelial tissue of peritoneum
D210	Benign neoplasm of conn & soft tiss of head, face and
D219	Benign neoplasm of conn & soft tiss, unspecified
D269	Other benign neoplasms of uterus, unspecified
D27X	Benign neoplasm of ovary
D300	Benign neoplasm of kidney
D303	Benign neoplasm of bladder
D320	Benign neoplasm of cerebral meninges
D321	Benign neoplasm of spinal meninges
D329	Benign neoplasm of meninges, unspecified
D330	Benign neoplasm of brain, supratentorial
D332	Benign neoplasm of brain, unspecified
D333	Benign neoplasm of cranial nerves
D34X	Benign neoplasm of thyroid gland
D350	Benign neoplasm of adrenal gland
D351	Benign neoplasm of parathyroid gland
D352	Benign neoplasm of pituitary gland
D354	Benign neoplasm of pineal gland
D360	Benign neoplasm of lymph nodes
D361	Benign neoplasm of periph nerves & autonomic
D369	Benign neoplasm of unspecified site
D370	Neoplasm uncert / unkn behav lip, oral cavity and
D380	Neoplasm uncert / unkn behav larynx
D381	Neoplasm uncert / unkn behav trachea, bronchus and
D382	Neoplasm uncert / unkn behav pleura
D383	Neoplasm uncert / unkn behav mediastinum
D391	Neoplasm uncert / unkn behav ovary
D410	Neoplasm uncert / unkn behav kidney
D412	Neoplasm uncert / unkn behav ureter
D414	Neoplasm uncert / unkn behav bladder
D429	Neoplasm uncert / unkn behav meninges, unspecified
D430	Neoplasm uncert / unkn behav brain, supratentorial
D431	Neoplasm uncert / unkn behav brain, infratentorial
D432	Neoplasm uncert / unkn behav brain, unspecified
D440	Neoplasm uncert / unkn behav thyroid gland
D441	Neoplasm uncert / unkn behav adrenal gland
D443	Neoplasm uncert / unkn behav pituitary gland
D444	Neoplasm uncert / unkn behav craniopharyngeal duct
D447	Neoplasm uncert / unkn behav aortic body & oth
D448	Neoplasm uncert / unkn behav pluriglandular
D449	Neoplasm uncert / unkn behav endocrine gland,
D480	Neoplasm uncert or unknown behaviour of bone &
D481	Neoplasm uncert or unknown behaviour of conn &
D489	Neoplasm of uncertain or unknown behaviour,
G210	Malignant neuroleptic syndrome
H602	Malignant otitis externa
Q850	Neurofibromatosis (nonmalignant)
	Symptom codes
D500	Iron deficiency anaemia secondary to blood loss
D508	Other iron deficiency anaemias
D509	Iron deficiency anaemia, unspecified
D510	Vitamin B12 defic anaemia due to intrinsic factor
D513	Other dietary vitamin B12 deficiency anaemia
D518	Other vitamin B12 deficiency anaemias
D519	Vitamin B12 deficiency anaemia, unspecified
D520	Dietary folate deficiency anaemia
D521	Drug-induced folate deficiency anaemia
D528	Other folate deficiency anaemias
D529	Folate deficiency anaemia, unspecified
D531	Other megaloblastic anaemias, not elsewhere
D538	Other specified nutritional anaemias
D539	Nutritional anaemia, unspecified
D648	Other specified anaemias
D649	Anaemia, unspecified
E164	Abnormal secretion of gastrin Hypergastrinaemia
K30X	Dyspepsia
K920	Haematemesis
K921	Melaena
R071	Chest pain on breathing
R073	Other chest pain
R074	Chest pain, unspecified
R101	Pain localized to upper abdomen
R104	Other and unspecified abdominal pain
R11X	Nausea and vomiting
R12X	Heartburn
R13X	Dysphagia
R190	Intra-abdominal and pelvic swelling, mass and lump
R229	Localized swelling, mass and lump, unspecified
R529	Pain, unspecified
R630	Anorexia
R634	Abnormal weight loss
R933	Abn finds diagnostic imaging of oth parts of digestive
R935	Abn finds diag imaging oth abdo region inc
R938	Abn finds on diag imaging of other spec body
Z800	Family history of malignant neoplasm Family history
Z808	Family history of malignant neoplasm Family history
	Miscellaneous codes

Appendix 7.9 STROBE Statement

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Yes (see title and abstract page 5)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Yes (see INTRODUCTION summary boxes in chapter 1- and RATIONALE in chapter 2 page 87)
Objectives	3	State specific objectives, including any prespecified hypotheses Yes (see chapter 2 pages 88 and 89)
Methods		
Study design	4	Present key elements of study design early in the paper Yes (see main METHOD chapters 2 and 3 along with supporting appendices chapter 7)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Yes (see main METHOD section in chapters 2 and 3)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants Yes (see METHODS pages 111-115, 147, 188 and 191)
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Yes (see pages 97-100 and 150)
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Yes (See METHOD sections in chapter 2,3,4,5)

Bias	9	Describe any efforts to address potential sources of bias Yes (See method sections in chapters 3, 4, and 5. Mainly Sensitivity analysis section in chapter 4)
Study size	10	Explain how the study size was arrived at N/A All cases in a national cohort
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Yes (Method sections in Chapter 4 and 5)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses Yes (See Analytical Approach sections in pages 102, 148, 149, 188-190, and 193) notably under 'Sensitivity Analyses
Results		
Participants	13	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram Yes (summarised in early stages of each RESULTS section of chapters 3, 4 and 5)
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount) Yes (summarised in early stages of each RESULTS section of chapters 3, 4 and 5)
Outcome data	15	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures

		Yes (summarised in Tables 4.1-4.7, 5.1-5.4, and figures 5.4-5.5)
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Yes (See Tables and figures for crude and adjusted estimates in chapter 4)
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Yes (See sensitivity analysis result section in chapter 4)
Discussion		
Key results	18	Summarise key results with reference to study objectives Yes – See early stages of each discussion sections of chapters 3, 4 and 5
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Yes, See discussion section of chapters 3, 4, 5, and 6
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Yes, See general discussion section in chapter 6
Generalisability	21	Discuss the generalisability (external validity) of the study results Yes, local audit validation sections in chapter 3 and 5
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based YES – see the acknowledgment

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Syntax 7.1 Assign speciality type

This syntax was used to assign a Specialty Type of 1 for a surgical specialty and 2 for a medical specialty, based on the Specialty code (Mainspef) of the episode.

For 2006-07 data year there were 11,580,198 episodes. (Medical = 6.336.909 (54.7%), Surgical = 5,243,289 (45.3%) and for 2007-08 there were= 12,181,932 episodes. (Medical = 6,581,016 (54.0%), Surgical = 5,600,916 (46.0%)

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COMPUTE SPECIALTYTYPE = 0.
EXECUTE.
IF (MAINSPEF = 300|
MAINSPEF = 301|
MAINSPEF = 302|
MAINSPEF = 303|
MAINSPEF = 305|
MAINSPEF = 313|
MAINSPEF = 314|
MAINSPEF = 315|
MAINSPEF = 320|
MAINSPEF = 330|
MAINSPEF = 340|
MAINSPEF = 350|
MAINSPEF = 352|
MAINSPEF = 360|
MAINSPEF = 361|
MAINSPEF = 370|
MAINSPEF = 400|
MAINSPEF = 410|
MAINSPEF = 430|
MAINSPEF = 823)SPECIALTYTYPE = 2.
EXECUTE.

IF (MAINSPEF = 100|
MAINSPEF = 101|
MAINSPEF = 110|
MAINSPEF = 120|
MAINSPEF = 130|
MAINSPEF = 140|
MAINSPEF = 145|
MAINSPEF = 150|
MAINSPEF = 160|
MAINSPEF = 170|
MAINSPEF = 180|
MAINSPEF = 190|
MAINSPEF = 192)SPECIALTYTYPE = 1.
EXECUTE.
```

Syntax 7.2 Trust selection

```
COMPUTE TRUSTINC = 0.
EXECUTE.

IF (PROCODE = '5QT'|
PROCODE = 'RA2'|
PROCODE = 'RA3'|
PROCODE = 'RA4'|
PROCODE = 'RA7'|
PROCODE = 'RA9'|
PROCODE = 'RAE'|
PROCODE = 'RAJ'|
PROCODE = 'RAL'|
PROCODE = 'RAP'|
PROCODE = 'RAS'|
PROCODE = 'RAX'|
PROCODE = 'RBA'|
PROCODE = 'RBD'|
PROCODE = 'RBK'|
PROCODE = 'RBL'|
PROCODE = 'RBN'|
PROCODE = 'RBT'|
PROCODE = 'RBZ'|
PROCODE = 'RC1'|
PROCODE = 'RC3'|
PROCODE = 'RC9'|
PROCODE = 'RCB'|
PROCODE = 'RCC'|
PROCODE = 'RCD'|
PROCODE = 'RCF'|
PROCODE = 'RCX'|
PROCODE = 'RD1'|
PROCODE = 'RD3'|
PROCODE = 'RD7'|
PROCODE = 'RD8'|
PROCODE = 'RDD'|
PROCODE = 'RDE'|
PROCODE = 'RDU'|
PROCODE = 'RDZ'|
PROCODE = 'RE9'|
PROCODE = 'REF'|
PROCODE = 'REM'|
PROCODE = 'RF4'|
PROCODE = 'RFF'|
PROCODE = 'RFR'|
PROCODE = 'RFS'|
PROCODE = 'RFW'|
PROCODE = 'RG2'|
PROCODE = 'RG3'|
PROCODE = 'RGC'|
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PROCODE = 'RGP'|
PROCODE = 'RGQ'|
PROCODE = 'RGR'|
PROCODE = 'RGT'|
PROCODE = 'RGZ'|
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PROCODE = 'RHQ'|
PROCODE = 'RHU'|
PROCODE = 'RHW'|
PROCODE = 'RJ1'|
PROCODE = 'RJ2'|
PROCODE = 'RJ5'|
PROCODE = 'RJ6'|
PROCODE = 'RJ7'|
PROCODE = 'RJC'|
PROCODE = 'RJD'|
PROCODE = 'RJE'|
PROCODE = 'RJF'|
PROCODE = 'RJL'|
PROCODE = 'RJN'|
PROCODE = 'RJR'|
PROCODE = 'RJZ'|
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PROCODE = 'RK9'|
PROCODE = 'RKB'|
PROCODE = 'RKE'|
PROCODE = 'RL4'|
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PROCODE = 'RLQ'|
PROCODE = 'RLT'|
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PROCODE = 'RNJ'|
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PROCODE = 'RNQ'|
PROCODE = 'RNS'|
PROCODE = 'RNZ'|
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PROCODE = 'RQQ'|
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PROCODE = 'RWJ'|
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PROCODE = 'RX1'|
PROCODE = 'RXC'|
PROCODE = 'RXF'|
PROCODE = 'RXH'|
PROCODE = 'RXK'|
PROCODE = 'RXL'|
PROCODE = 'RXN'|
PROCODE = 'RXP'|
PROCODE = 'RXQ'|
PROCODE = 'RXR'|
PROCODE = 'RXW'|
PROCODE = 'RYJ')TRUSTINC = 1.
EXECUTE.
```

Syntax 7.3 OG cancer syntax

```
COMPUTE CANCER1 = 0.
EXECUTE.
IF (DIAG01 = "C169"|
DIAG01 = "C160"|
DIAG01 = "C161"|
DIAG01 = "C162"|
DIAG01 = "C163"|
DIAG01 = "C164"|
DIAG01 = "C165"|
DIAG01 = "C166"|
DIAG01 = "C168"|
DIAG01 = "C159"|
DIAG01 = "C158"|
DIAG01 = "C150"|
DIAG01 = "C151"|
DIAG01 = "C152"|
DIAG01 = "C153"|
DIAG01 = "C154"|
DIAG01 = "C155")CANCER1 = 1.
EXECUTE.
```

The same syntax was applied to identify these codes in other diagnostic position (DIAG02 to DIAG 14)

Then these 14 new variables (CANCER1 + CANCER2+…..+CANCER14) were added and a new variable called **OGCANCER** was created which then updated by the following syntax to develop a binary variable that show whether the patients (episodes) had been coded with any of these codes or not.

```
COMPUTE HaveOGCANCER = 0.
EXECUTE.
IF (OGCANCER > 0)HaveOGCANCER = 1.
EXECUTE.
```

Syntax 7.4 Diagnostic gastroscopy syntax

```
COMPUTE GASTROSCOPYpro1 = 0.
EXECUTE.
if(OPERTN1 = 'G451'|
OPERTN1 = 'G459'|
OPERTN1 = 'G45'|
OPERTN1 = 'G169'|
OPERTN1 = 'G458'|
OPERTN1 = 'G161'|
OPERTN1 = 'G16'|
OPERTN1 = 'G168'|
OPERTN1 = 'G454')GASTROSCOPYpro1 = 1.
EXECUTE .
```

The same syntax was applied to identify these codes in other diagnostic position (OPERTN02 to OPERTN14)

Then these 14 new variables (GASTROSCOPYpro1 + GASTROSCOPYpro2+…..+ GASTROSCOPYpro14) were added and a new variable called **diagnostic gastroscopy** was created which then updated by the following syntax to develop a binary variable that show whether the patients (episodes) had been coded with any of these codes or not.

```
COMPUTE HaveGASTROSCOPY = 0.
EXECUTE.
IF (diagnostic gastroscopy > 0)HaveGASTROSCOPY = 1.
EXECUTE.
```

Identification of the first Gastroscopy procedure date (FGD)

This process commenced by selecting all patients in 2006/08 merged OGC patients' episodes dataset who have had a diagnostic gastroscopy in PROCEDURE 1 position and Create a field called diagnostic gastroscopy DATE and update to equal the PRODATE 1 (i.e. procedure date at position 1); the resulted file need to be saved as separate dataset,(Doing the same action for PROCEDURE positions 2 to 14, each time creating a separate dataset, and then creating a field called diagnostic gastroscopy DATE which should equal its PRODATE) then by merging all 14 datasets together (all dataset variables should be in the same order with the same variable names and format before the merge) by that the diagnostic gastroscopy DATE variable will have the date of every diagnostic procedure code in every episode of care in one column. After that, using the "identify duplicate cases" function in SPSS, the chronologically first episode of care containing the first episode for each patient was flagged with a new variable (PRIMARYFIRST=1). Then the last episode was also flagged with another new variable (PRIMARYLAST=1). These two new variables represent the first and the last diagnostic gastroscopy that each patient have had in his or her management journey along with their date.

Syntax 7.5 Identification of the first OG cancer coding date (FOGCD)

The processes commences by first, 'Sorting' the data by the patients' HESID and date of admissions in ascending order. Then using the "identify duplicate cases" function in SPSS, the chronologically first episode of care containing the first admission date for each patient will be flagged with a new variable (PRIMARYFIRST=1). Using the Select function to copy the PRIMARYFIRST=1 into a new dataset. From the resulted data, copy "episode end date" variable along with the patients' HESID into another new dataset and rename the "episode end date" to be "OGC 1^{ST} episode end date", then save the resulted file as "0608 OGC patients' first episode end date". Following that, this new variable can be added to the main OG cancer dataset using SPSS function: DATA > MERGE FILE > ADD VARIABLE.

By calculation the number of days between the first OG cancer coding date (FOGCD) and the first Gastroscopy procedure date (FGD) and by using the following syntax we extracted a cohort of patients with a sequence of care episodes and diagnostic procedures compatible with a new diagnosis of OG cancer.

```
COMPUTE STUDYGROUP = 0.
EXECUTE.
IF (number of days between the (FOGCD) and the (FGD) ≥0 & number of days between the (FOGCD)
and the (FGD)  ≤90) STUDYGROUPS = 1.
EXECUTE.
```

OG cancer incidence cases selection syntax

```
COMPUTE STUDYGROUPS = 0.
EXECUTE.
IF (FirstOGcancerCodingDate_MINUS_FirstGastroscopyDate = 0) STUDYGROUPS = 1.
EXECUTE.
IF (FirstOGcancerCodingDate_MINUS_FirstGastroscopyDate  >0 &
FirstOGcancerCodingDate_MINUS_FirstGastroscopyDate <=90) STUDYGROUPS = 2.
EXECUTE.
IF (FirstOGcancerCodingDate_MINUS_FirstGastroscopyDate >90) STUDYGROUPS = 3.
EXECUTE.
IF (FirstOGcancerCodingDate_MINUS_FirstGastroscopyDate <0) STUDYGROUPS = 4.
EXECUTE.
```

Syntax 7.6 Patients' age group syntax

```
COMPUTE AGEGROUP = 0.
EXECUTE.
IF (ENDAGE < 55) AGEGROUP = 1.
EXECUTE.
IF (ENDAGE > 54 & ENDAGE < 65) AGEGROUP = 2.
EXECUTE.
IF (ENDAGE > 64 & ENDAGE <75) AGEGROUP = 3.
EXECUTE.
IF (ENDAGE >74 & ENDAGE <85) AGEGROUP = 4.
EXECUTE.
IF (ENDAGE >84) AGEGROUP = 5.
EXECUTE.
```

Syntax 7.7 Comorbidity syntax (charson's scores)

```
COMPUTE COMORBID1 = 0.

EXECUTE.

IF (DIAG01 = 'E101'|DIAG01 = 'E105'|DIAG01 = 'E109'|DIAG01 = 'E111'|DIAG01 = 'E115'|DIAG01 =
'E119'|DIAG01 = 'E131'|DIAG01 = 'E135'|DIAG01 = 'E139'|DIAG01 = 'E141'|DIAG01 = 'E145'|DIAG01
= 'E149'|DIAG01 = 'F000'|DIAG01 = 'F001'|DIAG01 = 'F002'|DIAG01 = 'F009'|DIAG01 =
'F010'|DIAG01 = 'F011'|DIAG01 = 'F012'|DIAG01 = 'F013'|DIAG01 = 'F018'|DIAG01 = 'F019'|DIAG01
= 'F020'|DIAG01 = 'F021'|DIAG01 = 'F022'|DIAG01 = 'F023'|DIAG01 = 'F024'|DIAG01 =
'F028'|DIAG01 = 'F051'|DIAG01 = 'G450'|DIAG01 = 'G451'|DIAG01 = 'G452'|DIAG01 =
'G454'|DIAG01 = 'G458'|DIAG01 = 'G459'|DIAG01 = 'G460'|DIAG01 = 'G461'|DIAG01 =
'G462'|DIAG01 = 'G463'|DIAG01 = 'G464'|DIAG01 = 'G465'|DIAG01 = 'G466'|DIAG01 =
'G467'|DIAG01 = 'G468'|DIAG01 = 'I210'|DIAG01 = 'I211'|DIAG01 = 'I212'|DIAG01 = 'I213'|DIAG01 =
'I214'|DIAG01 = 'I219'|DIAG01 = 'I220'|DIAG01 = 'I221'|DIAG01 = 'I228'|DIAG01 = 'I229'|DIAG01 =
'I252'|DIAG01 = 'I500'|DIAG01 = 'I501'|DIAG01 = 'I509'|DIAG01 = 'I601'|DIAG01 = 'I602'|DIAG01 =
'I603'|DIAG01 = 'I604'|DIAG01 = 'I605'|DIAG01 = 'I606'|DIAG01 = 'I607'|DIAG01 = 'I608'|DIAG01 =
'I609'|DIAG01 = 'I610'|DIAG01 = 'I611'|DIAG01 = 'I612'|DIAG01 = 'I613'|DIAG01 = 'I614'|DIAG01 =
'I615'|DIAG01 = 'I616'|DIAG01 = 'I618'|DIAG01 = 'I619'|DIAG01 = 'I620'|DIAG01 = 'I621'|DIAG01 =
'I629'|DIAG01 = 'I630'|DIAG01 = 'I631'|DIAG01 = 'I632'|DIAG01 = 'I633'|DIAG01 = 'I634'|DIAG01 =
'I635'|DIAG01 = 'I636'|DIAG01 = 'I638'|DIAG01 = 'I639'|DIAG01 = 'I64X'|DIAG01 = 'I650'|DIAG01 =
'I651'|DIAG01 = 'I652'|DIAG01 = 'I653'|DIAG01 = 'I658'|DIAG01 = 'I659'|DIAG01 = 'I660'|DIAG01 =
'I661'|DIAG01 = 'I662'|DIAG01 = 'I663'|DIAG01 = 'I664'|DIAG01 = 'I668'|DIAG01 = 'I669'|DIAG01 =
'I670'|DIAG01 = 'I671'|DIAG01 = 'I672'|DIAG01 = 'I674'|DIAG01 = 'I675'|DIAG01 = 'I676'|DIAG01 =
'I677'|DIAG01 = 'I678'|DIAG01 = 'I679'|DIAG01 = 'I681'|DIAG01 = 'I682'|DIAG01 = 'I688'|DIAG01 =
'I690'|DIAG01 = 'I691'|DIAG01 = 'I692'|DIAG01 = 'I693'|DIAG01 = 'I694'|DIAG01 = 'I698'|DIAG01 =
'I710'|DIAG01 = 'I711'|DIAG01 = 'I712'|DIAG01 = 'I713'|DIAG01 = 'I714'|DIAG01 = 'I715'|DIAG01 =
'I716'|DIAG01 = 'I718'|DIAG01 = 'I719'|DIAG01 = 'I739'|DIAG01 = 'I790'|DIAG01 = 'J450'|DIAG01 =
'J451'|DIAG01 = 'J458'|DIAG01 = 'J459'|DIAG01 = 'J46X'|DIAG01 = 'J47X'|DIAG01 = 'J60X'|DIAG01 =
'J61X'|DIAG01 = 'J620'|DIAG01 = 'J628'|DIAG01 = 'J630'|DIAG01 = 'J631'|DIAG01 = 'J632'|DIAG01 =
'J633'|DIAG01 = 'J634'|DIAG01 = 'J635'|DIAG01 = 'J638'|DIAG01 = 'J64X'|DIAG01 = 'J65X'|DIAG01 =
'J660'|DIAG01 = 'J661'|DIAG01 = 'J662'|DIAG01 = 'J668'|DIAG01 = 'K250'|DIAG01 = 'K251'|DIAG01 =
'K252'|DIAG01 = 'K253'|DIAG01 = 'K254'|DIAG01 = 'K255'|DIAG01 = 'K256'|DIAG01 = 'K257'|DIAG01
= 'K259'|DIAG01 = 'K260'|DIAG01 = 'K261'|DIAG01 = 'K262'|DIAG01 = 'K263'|DIAG01 =
'K264'|DIAG01 = 'K265'|DIAG01 = 'K266'|DIAG01 = 'K267'|DIAG01 = 'K269'|DIAG01 = 'K270'|DIAG01
= 'K271'|DIAG01 = 'K272'|DIAG01 = 'K273'|DIAG01 = 'K274'|DIAG01 = 'K275'|DIAG01 =
'K276'|DIAG01 = 'K277'|DIAG01 = 'K279'|DIAG01 = 'K280'|DIAG01 = 'K281'|DIAG01 = 'K282'|DIAG01
= 'K283'|DIAG01 = 'K284'|DIAG01 = 'K285'|DIAG01 = 'K286'|DIAG01 = 'K287'|DIAG01 =
'K289'|DIAG01 = 'K702'|DIAG01 = 'K703'|DIAG01 = 'K717'|DIAG01 = 'K731'|DIAG01 = 'K732'|DIAG01
= 'K738'|DIAG01 = 'K739'|DIAG01 = 'K740'|DIAG01 = 'K742'|DIAG01 = 'K743'|DIAG01 =
```

'K744'|DIAG01 = 'K745'|DIAG01 = 'K746'|DIAG01 = 'M050'|DIAG01 = 'M051'|DIAG01 =
'M052'|DIAG01 = 'M053'|DIAG01 = 'M058'|DIAG01 = 'M059'|DIAG01 = 'M060'|DIAG01 =
'M063'|DIAG01 = 'M069'|DIAG01 = 'M320'|DIAG01 = 'M321'|DIAG01 = 'M328'|DIAG01 =
'M329'|DIAG01 = 'M332'|DIAG01 = 'M340'|DIAG01 = 'M341'|DIAG01 = 'M342'|DIAG01 =
'M348'|DIAG01 = 'M349'|DIAG01 = 'M353'|DIAG01 = 'R02X'|DIAG01 = 'Z958'|DIAG01 =
'Z959')COMORBID1 = 1.

EXECUTE.

IF (DIAG01 = 'C000'|DIAG01 = 'C001'|DIAG01 = 'C002'|DIAG01 = 'C003'|DIAG01 = 'C004'|DIAG01 =
'C005'|DIAG01 = 'C006'|DIAG01 = 'C008'|DIAG01 = 'C009'|DIAG01 = 'C01X'|DIAG01 =
'C020'|DIAG01 = 'C021'|DIAG01 = 'C022'|DIAG01 = 'C023'|DIAG01 = 'C024'|DIAG01 =
'C028'|DIAG01 = 'C029'|DIAG01 = 'C030'|DIAG01 = 'C031'|DIAG01 = 'C039'|DIAG01 =
'C040'|DIAG01 = 'C041'|DIAG01 = 'C048'|DIAG01 = 'C049'|DIAG01 = 'C050'|DIAG01 =
'C051'|DIAG01 = 'C052'|DIAG01 = 'C058'|DIAG01 = 'C059'|DIAG01 = 'C060'|DIAG01 =
'C061'|DIAG01 = 'C062'|DIAG01 = 'C068'|DIAG01 = 'C069'|DIAG01 = 'C07X'|DIAG01 =
'C080'|DIAG01 = 'C081'|DIAG01 = 'C088'|DIAG01 = 'C089'|DIAG01 = 'C090'|DIAG01 =
'C091'|DIAG01 = 'C098'|DIAG01 = 'C099'|DIAG01 = 'C100'|DIAG01 = 'C101'|DIAG01 =
'C102'|DIAG01 = 'C103'|DIAG01 = 'C104'|DIAG01 = 'C108'|DIAG01 = 'C109'|DIAG01 =
'C110'|DIAG01 = 'C111'|DIAG01 = 'C112'|DIAG01 = 'C113'|DIAG01 = 'C118'|DIAG01 =
'C119'|DIAG01 = 'C12X'|DIAG01 = 'C130'|DIAG01 = 'C131'|DIAG01 = 'C132'|DIAG01 =
'C138'|DIAG01 = 'C139'|DIAG01 = 'C140'|DIAG01 = 'C142'|DIAG01 = 'C148'|

DIAG01 = 'C170'|DIAG01 = 'C171'|DIAG01 = 'C172'|DIAG01 = 'C173'|DIAG01 = 'C178'|DIAG01 =
'C179'|DIAG01 = 'C180'|DIAG01 = 'C181'|DIAG01 = 'C182'|DIAG01 = 'C183'|DIAG01 =
'C184'|DIAG01 = 'C185'|DIAG01 = 'C186'|DIAG01 = 'C187'|DIAG01 = 'C188'|DIAG01 =
'C189'|DIAG01 = 'C19X'|DIAG01 = 'C20X'|DIAG01 = 'C210'|DIAG01 = 'C211'|DIAG01 =
'C212'|DIAG01 = 'C218'|DIAG01 = 'C220'|DIAG01 = 'C221'|DIAG01 = 'C222'|DIAG01 =
'C223'|DIAG01 = 'C224'|DIAG01 = 'C227'|DIAG01 = 'C229'|DIAG01 = 'C23X'|DIAG01 =
'C240'|DIAG01 = 'C241'|DIAG01 = 'C248'|DIAG01 = 'C249'|DIAG01 = 'C250'|DIAG01 =
'C251'|DIAG01 = 'C252'|DIAG01 = 'C253'|DIAG01 = 'C254'|DIAG01 = 'C257'|DIAG01 =
'C258'|DIAG01 = 'C259'|DIAG01 = 'C260'|DIAG01 = 'C261'|DIAG01 = 'C268'|DIAG01 =
'C269'|DIAG01 = 'C300'|DIAG01 = 'C301'|DIAG01 = 'C310'|DIAG01 = 'C311'|DIAG01 =
'C312'|DIAG01 = 'C313'|DIAG01 = 'C318'|DIAG01 = 'C319'|DIAG01 = 'C320'|DIAG01 =
'C321'|DIAG01 = 'C322'|DIAG01 = 'C323'|DIAG01 = 'C328'|DIAG01 = 'C329'|DIAG01 =
'C33X'|DIAG01 = 'C340'|DIAG01 = 'C341'|DIAG01 = 'C342'|DIAG01 = 'C343'|DIAG01 =
'C348'|DIAG01 = 'C349'|DIAG01 = 'C37X'|DIAG01 = 'C380'|DIAG01 = 'C381'|DIAG01 =
'C382'|DIAG01 = 'C383'|DIAG01 = 'C384'|DIAG01 = 'C388'|DIAG01 = 'C390'|DIAG01 =
'C398'|DIAG01 = 'C399'|DIAG01 = 'C400'|DIAG01 = 'C401'|DIAG01 = 'C402'|DIAG01 =
'C403'|DIAG01 = 'C408'|DIAG01 = 'C409'|DIAG01 = 'C410'|DIAG01 = 'C411'|DIAG01 =
'C412'|DIAG01 = 'C413'|DIAG01 = 'C414'|DIAG01 = 'C418'|DIAG01 = 'C419'|DIAG01 =
'C430'|DIAG01 = 'C431'|DIAG01 = 'C432'|DIAG01 = 'C433'|DIAG01 = 'C434'|DIAG01 =
'C435'|DIAG01 = 'C436'|DIAG01 = 'C437'|DIAG01 = 'C438'|DIAG01 = 'C439'|DIAG01 =
'C450'|DIAG01 = 'C451'|DIAG01 = 'C452'|DIAG01 = 'C457'|DIAG01 = 'C459'|DIAG01 =
'C460'|DIAG01 = 'C461'|DIAG01 = 'C462'|DIAG01 = 'C463'|DIAG01 = 'C467'|DIAG01 =
'C468'|DIAG01 = 'C469'|DIAG01 = 'C470'|DIAG01 = 'C471'|DIAG01 = 'C472'|DIAG01 =
'C473'|DIAG01 = 'C474'|DIAG01 = 'C475'|DIAG01 = 'C476'|DIAG01 = 'C478'|DIAG01 =
'C479'|DIAG01 = 'C480'|DIAG01 = 'C481'|DIAG01 = 'C482'|DIAG01 = 'C488'|DIAG01 =
'C490'|DIAG01 = 'C491'|DIAG01 = 'C492'|DIAG01 = 'C493'|DIAG01 = 'C494'|DIAG01 =
'C495'|DIAG01 = 'C496'|DIAG01 = 'C498'|DIAG01 = 'C499'|DIAG01 = 'C500'|DIAG01 =
'C501'|DIAG01 = 'C502'|DIAG01 = 'C503'|DIAG01 = 'C504'|DIAG01 = 'C505'|DIAG01 =
'C506'|DIAG01 = 'C508'|DIAG01 = 'C509'|DIAG01 = 'C510'|DIAG01 = 'C511'|DIAG01 =
'C512'|DIAG01 = 'C518'|DIAG01 = 'C519'|DIAG01 = 'C52X'|DIAG01 = 'C530'|DIAG01 =
'C531'|DIAG01 = 'C538'|DIAG01 = 'C539'|DIAG01 = 'C540'|DIAG01 = 'C541'|DIAG01 =
'C542'|DIAG01 = 'C543'|DIAG01 = 'C548'|DIAG01 = 'C549'|DIAG01 = 'C55X'|DIAG01 =
'C56X'|DIAG01 = 'C570'|DIAG01 = 'C571'|DIAG01 = 'C572'|DIAG01 = 'C573'|DIAG01 =

```
'C574'|DIAG01 = 'C577'|DIAG01 = 'C578'|DIAG01 = 'C579'|DIAG01 = 'C58X'|DIAG01 =
'C600'|DIAG01 = 'C601'|DIAG01 = 'C602'|DIAG01 = 'C608'|DIAG01 = 'C609'|DIAG01 =
'C61X'|DIAG01 = 'C620'|DIAG01 = 'C621'|DIAG01 = 'C629'|DIAG01 = 'C630'|DIAG01 =
'C631'|DIAG01 = 'C632'|DIAG01 = 'C637'|DIAG01 = 'C638'|DIAG01 = 'C639'|DIAG01 =
'C64X'|DIAG01 = 'C65X'|DIAG01 = 'C66X'|DIAG01 = 'C670'|DIAG01 = 'C671'|DIAG01 =
'C672'|DIAG01 = 'C673'|DIAG01 = 'C674'|DIAG01 = 'C675'|DIAG01 = 'C676'|DIAG01 =
'C677'|DIAG01 = 'C678'|DIAG01 = 'C679'|DIAG01 = 'C680'|DIAG01 = 'C681'|DIAG01 =
'C688'|DIAG01 = 'C689'|DIAG01 = 'C690'|DIAG01 = 'C691'|DIAG01 = 'C692'|DIAG01 =
'C693'|DIAG01 = 'C694'|DIAG01 = 'C695'|DIAG01 = 'C696'|DIAG01 = 'C698'|DIAG01 =
'C699'|DIAG01 = 'C700'|DIAG01 = 'C701'|DIAG01 = 'C709'|DIAG01 = 'C710'|DIAG01 =
'C711'|DIAG01 = 'C712'|DIAG01 = 'C713'|DIAG01 = 'C714'|DIAG01 = 'C715'|DIAG01 =
'C716'|DIAG01 = 'C717'|DIAG01 = 'C718'|DIAG01 = 'C719'|DIAG01 = 'C720'|DIAG01 =
'C721'|DIAG01 = 'C722'|DIAG01 = 'C723'|DIAG01 = 'C724'|DIAG01 = 'C725'|DIAG01 =
'C728'|DIAG01 = 'C729'|DIAG01 = 'C73X'|DIAG01 = 'C740'|DIAG01 = 'C741'|DIAG01 =
'C749'|DIAG01 = 'C750'|DIAG01 = 'C751'|DIAG01 = 'C752'|DIAG01 = 'C753'|DIAG01 =
'C754'|DIAG01 = 'C755'|DIAG01 = 'C758'|DIAG01 = 'C759'|DIAG01 = 'C760'|DIAG01 =
'C761'|DIAG01 = 'C762'|DIAG01 = 'C763'|DIAG01 = 'C764'|DIAG01 = 'C765'|DIAG01 =
'C767'|DIAG01 = 'C768'|DIAG01 = 'C810'|DIAG01 = 'C811'|DIAG01 = 'C812'|DIAG01 =
'C813'|DIAG01 = 'C817'|DIAG01 = 'C819'|DIAG01 = 'C820'|DIAG01 = 'C821'|DIAG01 =
'C822'|DIAG01 = 'C827'|DIAG01 = 'C829'|DIAG01 = 'C830'|DIAG01 = 'C831'|DIAG01 =
'C832'|DIAG01 = 'C833'|DIAG01 = 'C834'|DIAG01 = 'C835'|DIAG01 = 'C836'|DIAG01 =
'C837'|DIAG01 = 'C838'|DIAG01 = 'C839'|DIAG01 = 'C840'|DIAG01 = 'C841'|DIAG01 =
'C842'|DIAG01 = 'C843'|DIAG01 = 'C844'|DIAG01 = 'C845'|DIAG01 = 'C850'|DIAG01 =
'C851'|DIAG01 = 'C857'|DIAG01 = 'C859'|DIAG01 = 'C883'|DIAG01 = 'C887'|DIAG01 =
'C889'|DIAG01 = 'C900'|DIAG01 = 'C901'|DIAG01 = 'C910'|DIAG01 = 'C911'|DIAG01 =
'C912'|DIAG01 = 'C913'|DIAG01 = 'C914'|DIAG01 = 'C915'|DIAG01 = 'C917'|DIAG01 =
'C919'|DIAG01 = 'C920'|DIAG01 = 'C921'|DIAG01 = 'C922'|DIAG01 = 'C923'|DIAG01 =
'C924'|DIAG01 = 'C925'|DIAG01 = 'C927'|DIAG01 = 'C929'|DIAG01 = 'C930'|DIAG01 =
'C931'|DIAG01 = 'C932'|DIAG01 = 'C937'|DIAG01 = 'C939'|DIAG01 = 'C940'|DIAG01 =
'C941'|DIAG01 = 'C942'|DIAG01 = 'C943'|DIAG01 = 'C945'|DIAG01 = 'C947'|DIAG01 =
'C950'|DIAG01 = 'C951'|DIAG01 = 'C952'|DIAG01 = 'C957'|DIAG01 = 'C959'|DIAG01 =
'C960'|DIAG01 = 'C961'|DIAG01 = 'C962'|DIAG01 = 'C963'|DIAG01 = 'C967'|DIAG01 =
'C969'|DIAG01 = 'E102'|DIAG01 = 'E103'|DIAG01 = 'E104'|DIAG01 = 'E112'|DIAG01 = 'E113'|DIAG01
= 'E114'|DIAG01 = 'E132'|DIAG01 = 'E133'|DIAG01 = 'E134'|DIAG01 = 'E142'|DIAG01 =
'E143'|DIAG01 = 'E144'|DIAG01 = 'G041'|DIAG01 = 'G810'|DIAG01 = 'G811'|DIAG01 =
'G819'|DIAG01 = 'G820'|DIAG01 = 'G821'|DIAG01 = 'G822'|DIAG01 = 'N010'|DIAG01 =
'N011'|DIAG01 = 'N012'|DIAG01 = 'N013'|DIAG01 = 'N014'|DIAG01 = 'N015'|DIAG01 =
'N016'|DIAG01 = 'N017'|DIAG01 = 'N018'|DIAG01 = 'N019'|DIAG01 = 'N031'|DIAG01 =
'N032'|DIAG01 = 'N033'|DIAG01 = 'N034'|DIAG01 = 'N035'|DIAG01 = 'N036'|DIAG01 =
'N037'|DIAG01 = 'N038'|DIAG01 = 'N039'|DIAG01 = 'N052'|DIAG01 = 'N053'|DIAG01 =
'N054'|DIAG01 = 'N055'|DIAG01 = 'N056'|DIAG01 = 'N072'|DIAG01 = 'N073'|DIAG01 =
'N074'|DIAG01 = 'N180'|DIAG01 = 'N188'|DIAG01 = 'N189'|DIAG01 = 'N19X'|DIAG01 =
'N250'|DIAG01 = 'N251'|DIAG01 = 'N258'|DIAG01 = 'N259')COMORBID1 = 2.

EXECUTE.

IF (DIAG01 = 'C770'|DIAG01 = 'C771'|DIAG01 = 'C772'|DIAG01 = 'C773'|DIAG01 = 'C774'|DIAG01 =
'C775'|DIAG01 = 'C778'|DIAG01 = 'C779'|DIAG01 = 'C780'|DIAG01 = 'C781'|DIAG01 =
'C782'|DIAG01 = 'C783'|DIAG01 = 'C784'|DIAG01 = 'C785'|DIAG01 = 'C786'|DIAG01 =
'C787'|DIAG01 = 'C788'|DIAG01 = 'C790'|DIAG01 = 'C791'|DIAG01 = 'C792'|DIAG01 =
'C793'|DIAG01 = 'C794'|DIAG01 = 'C795'|DIAG01 = 'C796'|DIAG01 = 'C797'|DIAG01 =
'C798'|DIAG01 = 'C80X'|DIAG01 = 'K721'|DIAG01 = 'K729'|DIAG01 = 'K766'|DIAG01 =
'K767')COMORBID1 = 3.

EXECUTE.
```

```
IF (DIAG01 = 'B200'|DIAG01 = 'B201'|DIAG01 = 'B202'|DIAG01 = 'B203'|DIAG01 = 'B204'|DIAG01 =
'B205'|DIAG01 = 'B206'|DIAG01 = 'B207'|DIAG01 = 'B208'|DIAG01 = 'B209'|DIAG01 =
'B210'|DIAG01 = 'B211'|DIAG01 = 'B212'|DIAG01 = 'B213'|DIAG01 = 'B217'|DIAG01 =
'B218'|DIAG01 = 'B219'|DIAG01 = 'B220'|DIAG01 = 'B221'|DIAG01 = 'B222'|DIAG01 =
'B227'|DIAG01 = 'B230'|DIAG01 = 'B231'|DIAG01 = 'B232'|DIAG01 = 'B238'|DIAG01 =
'B24X')COMORBID1 = 6.

EXECUTE.
```

The same syntax was applied to identify these codes in other diagnostic position (DIAG02 to DIAG 14)

Syntax 7.8 Comorbidity syntax

(present or not)

```
COMPUTE
NONCANCERCOMORB1 =
0.
EXECUTE.
IF (DIAG01 = 'I210'|
DIAG01 = 'I211'|
DIAG01 = 'I212'|
DIAG01 = 'I213'|
DIAG01 = 'I214'|
DIAG01 = 'I219'|
DIAG01 = 'I220'|
DIAG01 = 'I221'|
DIAG01 = 'I228'|
DIAG01 = 'I229'|
DIAG01 = 'I252'|
DIAG01 = 'I500'|
DIAG01 = 'I710'|
DIAG01 = 'I711'|
DIAG01 = 'I712'|
DIAG01 = 'I713'|
DIAG01 = 'I714'|
DIAG01 = 'I715'|
DIAG01 = 'I716'|
DIAG01 = 'I718'|
DIAG01 = 'I719'|
DIAG01 = 'I738'|
DIAG01 = 'I739'|
DIAG01 = 'I600'|
DIAG01 = 'I601'|
DIAG01 = 'I602'|
DIAG01 = 'I603'|
DIAG01 = 'I604'|
DIAG01 = 'I605'|
DIAG01 = 'I606'|
DIAG01 = 'I607'|
DIAG01 = 'I608'|
DIAG01 = 'I609'|
DIAG01 = 'I610'|
DIAG01 = 'I611'|
DIAG01 = 'I612'|
DIAG01 = 'I613'|
DIAG01 = 'I614'|
DIAG01 = 'I615'|
DIAG01 = 'I616'|
DIAG01 = 'I618'|
DIAG01 = 'I619'|
DIAG01 = 'I620'|
DIAG01 = 'I621'|
DIAG01 = 'I629'|
DIAG01 = 'I630'|
DIAG01 = 'I631'|
DIAG01 = 'I632'|
DIAG01 = 'I633'|
DIAG01 = 'I634'|
DIAG01 = 'I635'|
DIAG01 = 'I636'|
DIAG01 = 'I638'|
DIAG01 = 'I639'|
DIAG01 = 'I64X'|
DIAG01 = 'I650'|
DIAG01 = 'I651'|
DIAG01 = 'I652'|
DIAG01 = 'I653'|
DIAG01 = 'I658'|
DIAG01 = 'I659'|
DIAG01 = 'I660'|
DIAG01 = 'I661'|
DIAG01 = 'I662'|
DIAG01 = 'I663'|
DIAG01 = 'I664'|
DIAG01 = 'I668'|
DIAG01 = 'I669'|
DIAG01 = 'I670'|
DIAG01 = 'I671'|
DIAG01 = 'I672'|
DIAG01 = 'I673'|
DIAG01 = 'I674'|
DIAG01 = 'I675'|
DIAG01 = 'I676'|
DIAG01 = 'I677'|
DIAG01 = 'I678'|
DIAG01 = 'I679'|
DIAG01 = 'I680'|
DIAG01 = 'I681'|
DIAG01 = 'I682'|
DIAG01 = 'I688'|
DIAG01 = 'I690'|
DIAG01 = 'I691'|
DIAG01 = 'I692'|
DIAG01 = 'I693'|
DIAG01 = 'I694'|
DIAG01 = 'I698'|
DIAG01 = 'F000'|
DIAG01 = 'F001'|
DIAG01 = 'F002'|
DIAG01 = 'F009'|
DIAG01 = 'F010'|
DIAG01 = 'F011'|
DIAG01 = 'F012'|
DIAG01 = 'F013'|
DIAG01 = 'F018'|
DIAG01 = 'F019'|
DIAG01 = 'F020'|
DIAG01 = 'F021'|
DIAG01 = 'F022'|
DIAG01 = 'F023'|
DIAG01 = 'F024'|
DIAG01 = 'F028'|
DIAG01 = 'F03X'|
DIAG01 = 'F051'|
DIAG01 = 'J40X'|
DIAG01 = 'J410'|
DIAG01 = 'J411'|
DIAG01 = 'J418'|
```

DIAG01 = 'J42X'|
DIAG01 = 'J430'|
DIAG01 = 'J431'|
DIAG01 = 'J432'|
DIAG01 = 'J438'|
DIAG01 = 'J439'|
DIAG01 = 'J440'|
DIAG01 = 'J441'|
DIAG01 = 'J448'|
DIAG01 = 'J449'|
DIAG01 = 'J450'|
DIAG01 = 'J451'|
DIAG01 = 'J458'|
DIAG01 = 'J459'|
DIAG01 = 'J46X'|
DIAG01 = 'J47X'|
DIAG01 = 'J60X'|
DIAG01 = 'J61X'|
DIAG01 = 'J620'|
DIAG01 = 'J628'|
DIAG01 = 'J630'|
DIAG01 = 'J631'|
DIAG01 = 'J632'|
DIAG01 = 'J633'|
DIAG01 = 'J634'|
DIAG01 = 'J635'|
DIAG01 = 'J638'|
DIAG01 = 'J64X'|
DIAG01 = 'J65X'|
DIAG01 = 'J660'|
DIAG01 = 'J661'|
DIAG01 = 'J662'|
DIAG01 = 'J668'|
DIAG01 = 'J670'|
DIAG01 = 'J671'|
DIAG01 = 'J672'|
DIAG01 = 'J673'|
DIAG01 = 'J674'|
DIAG01 = 'J675'|
DIAG01 = 'J676'|
DIAG01 = 'J677'|
DIAG01 = 'J678'|
DIAG01 = 'J679'|
DIAG01 = 'M050'|
DIAG01 = 'M051'|
DIAG01 = 'M052'|
DIAG01 = 'M059'|
DIAG01 = 'M060'|
DIAG01 = 'M063'|
DIAG01 = 'M069'|
DIAG01 = 'M300'|
DIAG01 = 'M301'|
DIAG01 = 'M302'|
DIAG01 = 'M303'|
DIAG01 = 'M308'|
DIAG01 = 'M310'|
DIAG01 = 'M311'|
DIAG01 = 'M312'|
DIAG01 = 'M313'|
DIAG01 = 'M314'|
DIAG01 = 'M315'|
DIAG01 = 'M316'|
DIAG01 = 'M318'|
DIAG01 = 'M319'|
DIAG01 = 'M320'|
DIAG01 = 'M321'|
DIAG01 = 'M328'|
DIAG01 = 'M329'|
DIAG01 = 'M332'|
DIAG01 = 'M339'|
DIAG01 = 'M340'|
DIAG01 = 'M341'|
DIAG01 = 'M342'|
DIAG01 = 'M348'|
DIAG01 = 'M349'|
DIAG01 = 'M350'|
DIAG01 = 'M351'|
DIAG01 = 'M352'|
DIAG01 = 'M353'|
DIAG01 = 'M354'|
DIAG01 = 'M355'|
DIAG01 = 'M356'|
DIAG01 = 'M357'|
DIAG01 = 'K250'|
DIAG01 = 'K251'|
DIAG01 = 'K252'|
DIAG01 = 'K253'|
DIAG01 = 'K254'|
DIAG01 = 'K255'|
DIAG01 = 'K256'|
DIAG01 = 'K257'|
DIAG01 = 'K259'|
DIAG01 = 'K260'|
DIAG01 = 'K261'|
DIAG01 = 'K262'|
DIAG01 = 'K263'|
DIAG01 = 'K264'|
DIAG01 = 'K265'|
DIAG01 = 'K266'|
DIAG01 = 'K267'|
DIAG01 = 'K269'|
DIAG01 = 'K270'|
DIAG01 = 'K271'|
DIAG01 = 'K272'|
DIAG01 = 'K273'|
DIAG01 = 'K274'|
DIAG01 = 'K275'|
DIAG01 = 'K276'|
DIAG01 = 'K277'|
DIAG01 = 'K279'|
DIAG01 = 'K280'|
DIAG01 = 'K281'|
DIAG01 = 'K282'|
DIAG01 = 'K283'|
DIAG01 = 'K284'|
DIAG01 = 'K285'|
DIAG01 = 'K286'|
DIAG01 = 'K287'|
DIAG01 = 'K289'|
DIAG01 = 'K701'|
DIAG01 = 'K702'|
DIAG01 = 'K703'|
DIAG01 = 'K704'|
DIAG01 = 'K709'|
DIAG01 = 'K710'|
DIAG01 = 'K711'|
DIAG01 = 'K712'|
DIAG01 = 'K713'|
DIAG01 = 'K714'|
DIAG01 = 'K715'|
DIAG01 = 'K716'|
DIAG01 = 'K717'|
DIAG01 = 'K718'|
DIAG01 = 'K719'|
DIAG01 = 'K721'|
DIAG01 = 'K729'|
DIAG01 = 'K730'|
DIAG01 = 'K731'|
DIAG01 = 'K732'|
DIAG01 = 'K738'|
DIAG01 = 'K739'|
DIAG01 = 'K740'|
DIAG01 = 'K741'|
DIAG01 = 'K742'|
DIAG01 = 'K743'|
DIAG01 = 'K744'|
DIAG01 = 'K745'|
DIAG01 = 'K746'|
DIAG01 = 'K753'|
DIAG01 = 'K754'|
DIAG01 = 'K758'|
DIAG01 = 'K764'|
DIAG01 = 'K765'|
DIAG01 = 'K766'|
DIAG01 = 'K767'|
DIAG01 = 'K768'|
DIAG01 = 'E102'|
DIAG01 = 'E103'|
DIAG01 = 'E104'|
DIAG01 = 'E105'|
DIAG01 = 'E106'|
DIAG01 = 'E107'|
DIAG01 = 'E108'|
DIAG01 = 'E109'|
DIAG01 = 'E112'|
DIAG01 = 'E113'|
DIAG01 = 'E114'|
DIAG01 = 'E115'|

```
DIAG01 = 'E116'|
DIAG01 = 'E117'|
DIAG01 = 'E118'|
DIAG01 = 'E119'|
DIAG01 = 'E132'|
DIAG01 = 'E133'|
DIAG01 = 'E134'|
DIAG01 = 'E135'|
DIAG01 = 'E136'|
DIAG01 = 'E137'|
DIAG01 = 'E138'|
DIAG01 = 'E139'|
DIAG01 = 'E142'|
DIAG01 = 'E143'|
DIAG01 = 'E144'|
DIAG01 = 'E145'|
DIAG01 = 'E146'|
DIAG01 = 'E147'|
DIAG01 = 'E148'|
DIAG01 = 'E149'|
DIAG01 = 'G810'|
DIAG01 = 'G811'|
DIAG01 = 'G819'|
DIAG01 = 'G820'|
DIAG01 = 'G821'|
DIAG01 = 'G822'|
DIAG01 = 'N001'|
DIAG01 = 'N002'|
DIAG01 = 'N003'|
DIAG01 = 'N004'|
DIAG01 = 'N005'|
DIAG01 = 'N007'|
DIAG01 = 'N010'|
DIAG01 = 'N011'|
DIAG01 = 'N012'|
DIAG01 = 'N013'|
DIAG01 = 'N014'|
DIAG01 = 'N015'|
DIAG01 = 'N016'|
DIAG01 = 'N017'|
DIAG01 = 'N018'|
DIAG01 = 'N019'|
DIAG01 = 'N020'|
DIAG01 = 'N021'|
DIAG01 = 'N022'|
DIAG01 = 'N023'|
DIAG01 = 'N024'|
DIAG01 = 'N025'|
DIAG01 = 'N026'|
DIAG01 = 'N027'|
DIAG01 = 'N030'|
DIAG01 = 'N031'|
DIAG01 = 'N032'|
DIAG01 = 'N033'|
DIAG01 = 'N034'|
DIAG01 = 'N035'|
DIAG01 = 'N036'|
DIAG01 = 'N037'|
DIAG01 = 'N038'|
DIAG01 = 'N039'|
DIAG01 = 'N040'|
DIAG01 = 'N041'|
DIAG01 = 'N042'|
DIAG01 = 'N043'|
DIAG01 = 'N044'|
DIAG01 = 'N045'|
DIAG01 = 'N046'|
DIAG01 = 'N047'|
DIAG01 = 'N048'|
DIAG01 = 'N049'|
DIAG01 = 'N050'|
DIAG01 = 'N051'|
DIAG01 = 'N052'|
DIAG01 = 'N053'|
DIAG01 = 'N054'|
DIAG01 = 'N055'|
DIAG01 = 'N056'|
DIAG01 = 'N057'|
DIAG01 = 'N071'|
DIAG01 = 'N072'|
DIAG01 = 'N073'|
DIAG01 = 'N074'|
DIAG01 = 'N075'|
DIAG01 = 'N180'|
DIAG01 = 'N188'|
DIAG01 = 'N189'|
DIAG01 = 'N19X'|
DIAG01 = 'N250'|
DIAG01 = 'Z992'|
DIAG01 = 'B200'|
DIAG01 = 'B201'|
DIAG01 = 'B202'|
DIAG01 = 'B203'|
DIAG01 = 'B204'|
DIAG01 = 'B205'|
DIAG01 = 'B206'|
DIAG01 = 'B207'|
DIAG01 = 'B208'|
DIAG01 = 'B209'|
DIAG01 = 'B210'|
DIAG01 = 'B211'|
DIAG01 = 'B212'|
DIAG01 = 'B213'|
DIAG01 = 'B217'|
DIAG01 = 'B218'|
DIAG01 = 'B219'|
DIAG01 = 'B220'|
DIAG01 = 'B221'|
DIAG01 = 'B222'|
DIAG01 = 'B227'|
DIAG01 = 'B230'|
DIAG01 = 'B231'|
DIAG01 = 'B232'|
DIAG01 = 'B238'|
DIAG01 = 'B24X')NONCANCERCOMORB1 = 1.
EXECUTE.
```

The same syntax was applied to identify these codes in other diagnostic position (DIAG02 to DIAG 14) Then these 14 new variables (NONCANCERCOMORB1 + NONCANCERCOMORB2+…..+ NONCANCERCOMORB14) were added and a new variable called **AllComorbidity** was created which then updated by the following syntax to develop a binary variable that show whether the patients (episodes) had been coded with any of these codes or not.

```
COMPUTE HaveComorbidity = 0.
EXECUTE.
IF (AllComorbidity > 0)HaveComorbidity = 1.
EXECUTE.
```

Syntax 7.9 Comorbidity grouping syntax

```
COMPUTE comorbidityGROUPS = 0.
EXECUTE.
IF (AllComorbidity = 0) comorbidityGROUPS = 1.
EXECUTE.
IF (AllComorbidity =1) comorbidityGROUPS = 2.
EXECUTE.
IF (AllComorbidity >1) comorbidityGROUPS = 3.
EXECUTE.
```

Syntax 7.10 Deprivation grouping

The IMD score/rank has a range of 0 – 32482 which is based on Income, Employment, Health and Disability, Barriers to Housing, Crime and Living Environment within a postcode. Simply we have split the IMD scoring system 0 – 32482 into 5 parts, and developed the following syntax to assign a quintile to each Admission/patient, so we can analyse the level of deprivation the patients/disease actually fits into in the country.

```
COMPUTE NATDEPRIVQUINTILE = 0.
EXECUTE.
IF (DEPRIV < 6497)NATDEPRIVQUINTILE = 1.
EXECUTE.
IF (DEPRIV > 6496 & DEPRIV < 12993)NATDEPRIVQUINTILE = 2.
EXECUTE.
IF (DEPRIV > 12992 & DEPRIV < 19490)NATDEPRIVQUINTILE = 3.
EXECUTE.
IF (DEPRIV > 19489 & DEPRIV < 25986)NATDEPRIVQUINTILE = 4.
EXECUTE.
IF (DEPRIV > 25985 & DEPRIV < 32483)NATDEPRIVQUINTILE = 5.
EXECUTE.
```

Syntax 7.11 Admission methods syntax

This syntax was used to update a new variable called ADMISSMETHTYPE that is defines how the patient was admitted to hospital for the spell. First of all, the syntax creates a variable called ADMISSMETHTYPE and sets to 0, it then updates this variable dependant on what code is present in ADMIMETH. If ADMIMETH is equal to 11,12,13 then it is an ELECTIVE spell and ADMISSMETHTYPE is then updated to code 1. If ADMIMETH is equal to 21,22,23,24,28 then it is an EMERGENCY spell and ADMISSMETHTYPE is then updated to code 4. A new variable is now created called ADMMETHTYPE which will take the Admission type and the Patient Classification field which looks how the patient was managed into account. The syntax commands if ADMIMETHTYPE is equal to 1 and CLASS PAT is equal to 1 then update ADMMETHTYPE to 1, this means that this is an ELECTIVE ORDINARY admission. The syntax commands if ADMIMETHTYPE is equal to 81 then update ADMMETHTYPE to 1, this means that this is an ELECTIVE ORDINARY admission. The syntax commands if ADMIMETHTYPE is equal to 1 and CLASS PAT is equal to 2 then update ADMMETHTYPE to 2, this means that this is an ELECTIVE DAYCASE admission. The syntax commands if ADMIMETHTYPE is equal to 1 and CLASS PAT is equal to 3 and 4 then update ADMMETHTYPE to 3, this means that this is an ELECTIVE REGULAR ATTENDER admission. The syntax commands if ADMIMETHTYPE is equal to 4 then update ADMMETHTYPE to 4, this means that this is an EMERGENCY admission.

```
COMPUTE ADMISSMETHTYPE = 0 .
EXECUTE .
IF (ADMIMETH = 11|
ADMIMETH = 12|
ADMIMETH = 13)ADMISSMETHTYPE = 1.
EXECUTE .
IF (ADMIMETH = 21|
ADMIMETH = 22|
ADMIMETH = 23|
ADMIMETH = 24|
ADMIMETH = 28)ADMISSMETHTYPE = 4.
EXECUTE .
COMPUTE ADMMETHTYPE = 0 .
EXECUTE .
IF (ADMISSMETHTYPE= 1 &
CLASSPAT = 1) ADMMETHTYPE = 1 .
EXECUTE .
IF (ADMIMETH = 81) ADMMETHTYPE = 1 .
EXECUTE .
IF (ADMISSMETHTYPE= 1 &
CLASSPAT = 2) ADMMETHTYPE = 2 .
EXECUTE .
IF (ADMISSMETHTYPE= 1 &
CLASSPAT = 3) ADMMETHTYPE = 3 .
EXECUTE .
IF (ADMISSMETHTYPE= 1 &
CLASSPAT = 4) ADMMETHTYPE = 3 .
EXECUTE .
IF (ADMISSMETHTYPE= 4) ADMMETHTYPE = 4
.
EXECUTE .
```

Syntax 7.12 Major surgical resection syntax

```
COMPUTE SurgeryPro1 = 0.
EXECUTE.

if(OPERTN1 = 'G011'|
OPERTN1 = 'G281'|
OPERTN1 = 'G282'|
OPERTN1 = 'G283'|
OPERTN1 = 'G288'|
OPERTN1 = 'G029'|
OPERTN1 = 'G012'|
OPERTN1 = 'G013'|
OPERTN1 = 'G018'|
OPERTN1 = 'G019'|
OPERTN1 = 'G021'|
OPERTN1 = 'G022'|
OPERTN1 = 'G023'|
OPERTN1 = 'G024'|
OPERTN1 = 'G025'|
OPERTN1 = 'G028'|
OPERTN1 = 'G271'|
OPERTN1 = 'G272'|
OPERTN1 = 'G273'|
OPERTN1 = 'G274'|
OPERTN1 = 'G275'|
OPERTN1 = 'G278'|
OPERTN1 = 'G031'|
OPERTN1 = 'G032'|
OPERTN1 = 'G035'|
OPERTN1 = 'G036'|
OPERTN1 = 'G038'|
OPERTN1 = 'G039')SurgeryPro1 = 1.
EXECUTE.
```

The same syntax was applied to identify these codes in other diagnostic position (OPERTN02 to OPERTN14) Then these 14 new variables (SurgeryPro1 + SurgeryPro2+…..+ SurgeryPro14) were added and a new variable called **OG cancer Major resection** was created which then updated by the following syntax to develop a binary variable that show whether the patients (episodes) had been coded with any of these codes or not.

```
COMPUTE HaveMajorResection = 0.
EXECUTE.
IF (OG cancer Major resection > 0) HaveMajorResection = 1.EXECUTE.
```

Syntax 7.13 Thirty days and one year mortality syntax

```
COMPUTE mortality At ONE year = 0.
EXECUTE.
IF (diagnosisToDeath < 366) mortality At ONE year = 1.
EXECUTE.
COMPUTE mortality within 30 days = 0.
EXECUTE.
IF (diagnosisToDeath < 31) mortality within 30 days = 1.
EXECUTE.
```

Syntax 7.14 Age groups at first diagnostic gastroscopy syntax (for age standardization)

```
COMPUTE EndAgeAtGastroscopy15_19 = 0.
EXECUTE.
IF (ENDAGE_first >=15 & ENDAGE_first <=19)EndAgeAtGastroscopy15_19 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy20_24 = 0.
EXECUTE.
IF (ENDAGE_first >=20 & ENDAGE_first <=24)EndAgeAtGastroscopy20_24 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy25_29 = 0.
EXECUTE.
IF (ENDAGE_first >=25 & ENDAGE_first <=29)EndAgeAtGastroscopy25_29 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy30_34 = 0.
EXECUTE.
IF (ENDAGE_first >=30 & ENDAGE_first <=34)EndAgeAtGastroscopy30_34 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy35_39 = 0.
EXECUTE.
IF (ENDAGE_first >=35 & ENDAGE_first <=39)EndAgeAtGastroscopy35_39 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy40_44 = 0.
EXECUTE.
IF (ENDAGE_first >=40 & ENDAGE_first <=44)EndAgeAtGastroscopy40_44 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy45_49 = 0.
EXECUTE.
IF (ENDAGE_first >=45 & ENDAGE_first <=49)EndAgeAtGastroscopy45_49 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy50_54 = 0.
EXECUTE.
IF (ENDAGE_first >=50 & ENDAGE_first <=54)EndAgeAtGastroscopy50_54 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy55_59 = 0.
EXECUTE.
IF (ENDAGE_first >=55 & ENDAGE_first <=59)EndAgeAtGastroscopy55_59 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy60_64 = 0.
EXECUTE.
IF (ENDAGE_first >=60 & ENDAGE_first <=64)EndAgeAtGastroscopy60_64 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy65_69 = 0.
EXECUTE.
IF (ENDAGE_first >=65 & ENDAGE_first <=69)EndAgeAtGastroscopy65_69 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy70_74 = 0.
EXECUTE.
IF (ENDAGE_first >=70 & ENDAGE_first <=74)EndAgeAtGastroscopy70_74 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy75_79 = 0.
EXECUTE.
IF (ENDAGE_first >=75 & ENDAGE_first <=79)EndAgeAtGastroscopy75_79 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopy80_84 = 0.
EXECUTE.
IF (ENDAGE_first >=80 & ENDAGE_first <=84)EndAgeAtGastroscopy80_84 = 1.
EXECUTE .
COMPUTE EndAgeAtGastroscopyMorethan85 = 0.
EXECUTE.
IF (ENDAGE_first >84)EndAgeAtGastroscopyMorethan85 = 1.
EXECUTE .
```

Publication

This text box is where the unabridged thesis included the following third party copyrighted material:

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